Bibliografi Laboratory Acquired Infections: Antara Ancaman di Balik Kaca, Patogenesis Kompleks, dan Strategi Kontrol Infeksi Nosokomial dan Komunitas

PERPUSTAKAAN BALAI BESAR PERAKITAN DAN MODERNISASI VETERINER

BADAN PERAKITAN DAN MODERNISASI PERTANIAN

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Kata Pengantar

Laboratory Acquired Infections (LAIs) atau Infeksi yang Diperoleh di Laboratorium, menempati posisi unik sekaligus mengkhawatirkan dalam dunia kesehatan global. Infeksi-infeksi ini bukan hanya mencerminkan kegagalan prosedur biosekuriti di fasilitas penelitian dan diagnostik, tetapi juga menjadi jendela untuk memahami kompleksitas patogenesis infeksi, mekanisme resistensi antimikroba, dan tantangan dalam pengendalian infeksi di berbagai setting kesehatan. Bibliografi ini disusun untuk memetakan landskap penelitian mutakhir yang menghubungkan titik-temu antara ancaman di laboratorium, dinamika infeksi di rumah sakit (hospital-acquired), dan beban penyakit yang diperoleh di komunitas (community-acquired).

Kumpulan referensi dalam bibliografi ini merefleksikan beberapa tema kritis. **Pertama**, aspek fundamental patogenesis, seperti erosi penghalang mukosa dalam kolitis yang didapat, hingga adaptasi imun sel adiposa, menunjukkan bagaimana patogen memanipulasi inang, sebuah pengetahuan yang sangat relevan baik dalam konteks penelitian laboratorium maupun infeksi klinis. **Kedua**, tantangan global resistensi antimikroba (ESBL, AmpC, Carbapenemase) dan munculnya patogen hipervirulen, yang dilaporkan baik dalam infeksi saluran kemih komunitas di Sri Lanka maupun dalam wabah di rumah sakit di Ethiopia, menegaskan bahwa ancaman ini bersifat lintas batas—dari komunitas, ke rumah sakit, hingga laboratorium rujukan.

Ketiga, pandemi COVID-19 telah mengubah paradigma, tidak hanya sebagai penyakit komunitas yang menakutkan, tetapi juga sebagai faktor yang secara signifikan memengaruhi insiden dan outcome infeksi nosokomial, seperti yang terlihat pada data infeksi di ICU dan peningkatan infeksi bakteri/fungal sekunder pasca-terapi imunomodulator. **Keempat**, isu-isu khusus seperti infeksi yang didapat di laboratorium oleh *Brucella*, *Vibrio cholerae*, atau virus rekombinan, serta infeksi pada populasi rentan seperti pasien dengan hemofilia yang didapat atau koagulopati, menyoroti kerentanan spesifik dan kebutuhan protokol pencegahan yang ketat.

Bibliografi ini juga menyajikan perkembangan diagnostik, terapi, dan strategi pencegahan, mulai dari uji point-of-care untuk infeksi saluran pernapasan bawah, evaluasi antibiotik baru seperti omadacycline, terapi target seperti emicizumab untuk hemofilia A didapat, hingga pendekatan inovatif seperti tekstil antimikroba. Analisis berbasis *machine learning* untuk prediksi patogen dan penggunaan skor risiko baru yang dikembangkan dari *big data* rumah sakit menggambarkan arah masa depan dalam manajemen infeksi.

Diharapkan, kompilasi karya ilmiah dari berbagai belahan dunia—Tiongkok, Sri Lanka, Ethiopia, Prancis, Spanyol, Amerika Serikat, Australia, Nigeria, dan lainnya—ini dapat menjadi referensi yang komprehensif dan menarik bagi peneliti, ahli mikrobiologi, dokter, praktisi pengendalian infeksi, dan pembuat kebijakan. Pemahaman yang mendalam tentang interkoneksi antara LAIs, infeksi nosokomial, dan infeksi komunitas, beserta mekanisme molekuler dan epidemiologis yang mendasarinya, adalah kunci untuk merancang strategi pertahanan kesehatan yang lebih tangguh di masa depan.

Semoga bibliografi ini bermanfaat dan dapat memicu penelitian serta inovasi lebih lanjut dalam upaya kita bersama mengurangi beban penyakit infeksi yang diperoleh, di mana pun sumbernya.

DAFTAR ISI

1. **Innate mechanism of mucosal barrier erosion in the pathogenesis of acquired colitis**,Won Ho Yang, Peter V. Aziz, Douglas M. Heithoff, Yeolhoe Kim, Jeong Yeon Ko, Jin Won Cho, Michael J. Mahan, Markus Sperandio, Jamey D. Marth,iScience,Volume 26, Issue 10,2023,107883,https://doi.org/10.1016/j.isci.2023.107883.

Summary

The colonic mucosal barrier protects against infection, inflammation, and tissue ulceration. Composed primarily of Mucin-2, proteolytic erosion of this barrier is an invariant feature of colitis; however, the molecular mechanisms are not well understood. We have applied a recurrent food poisoning model of acquired inflammatory bowel disease using Salmonella enterica Typhimurium to investigate mucosal barrier erosion. Our findings reveal an innate Toll-like receptor 4-dependent mechanism activated by previous infection that induces Neu3 neuraminidase among colonic epithelial cells concurrent with increased Cathepsin-G protease secretion by Paneth cells. These anatomically separated host responses merge with the desialylation of nascent colonic Mucin-2 by Neu3 rendering the mucosal barrier susceptible to increased proteolytic breakdown by Cathepsin-G. Depletion of Cathepsin-G or Neu3 function using pharmacological inhibitors or genetic-null alleles protected against Mucin-2 proteolysis and barrier erosion and reduced the frequency and severity of colitis, revealing approaches to preserve and potentially restore the mucosal barrier.

Keywords: Biochemistry; Molecular biology; Immunology; Microbiology

2. **Phenotypic and genotypic distribution of ESBL, AmpC β-lactamase and carbapenemase-producing Enterobacteriaceae in community-acquired and hospital-acquired urinary tract infections in Sri Lanka**,Pandithage Dona Vindya Madushika Perera, Sirithilak Gamage, Hembadura Sara Melros De Silva, Sashika Kushlani Jayatilleke, Nelun de Silva, Alp Aydin, Virve I. Enne, Enoka Marie Corea,Journal of Global Antimicrobial Resistance,Volume 30,2022,Pages 115-122,https://doi.org/10.1016/j.jgar.2022.05.024.

Abstract:

Objectives

Although Sri Lanka belongs to a region with a high prevalence of extended-spectrum β-lactamase (ESBL), AmpC β-lactamase and carbapenemase-producing Enterobacteriaceae, data regarding antimicrobial resistance (AMR) is limited. We studied the prevalence and diversity of β-

lactamases produced by Enterobacteriaceae urinary pathogens from two hospitals in the Western Province of Sri Lanka.

Methods

ESBL, AmpC β-lactamase and carbapenemase production was detected by phenotypic testing followed by genotyping.

Results

The species responsible for urinary tract infections (UTI) were Escherichia coli (69%), Klebsiella pneumoniae (16%) and Enterobacter sp (6%). The prevalence of ESBL (50%), AmpC β-lactamase (19%) and carbapenemase (11%) phenotypes was high, and greater in hospital-acquired (HA-UTI) (75%) than in community-acquired UTI (CA-UTI) (42%). Identification of CA-UTI caused by carbapenemase-producing Enterobacteriaceae (5%) is alarming. Only one ESBL gene, blaCTX- M-15, was detected. AmpC β-lactamase genes found in E. coli and K. pneumoniae were blaCMY-2, blaCMY-42 and blaDHA-1, while Enterobacter sp. carried blaACT-1. Carbapenemase genes were blaNDM-1, blaNDM-4, blaOXA-181 and blaOXA-232, while blaKPC, blaIMP and blaVIM were absent. Co-occurrence of multiple bla genes, with some isolates harbouring six different bla genes, was common. Carbapenem-resistant isolates without carbapenemase genes displayed mutations in the outer membrane porin genes, ompF of E. coli and ompK36 of K. pneumoniae. Factors associated with UTI with β-lactamase-producing Enterobacteriaceae were age ≥50 years, previous hospitalization, presence of an indwelling urinary catheter, history of diabetes mellitus or other chronic illness and recurrent urinary tract infections.

Conclusion

This study adds to the currently scarce data on AMR in Sri Lanka.

Keywords: Extended-spectrum β-lactamase (ESBL); AmpC β-lactamase; Carbapenemase; Enterobacteriaceae; Urinary tract infections (UTI); Sri Lanka

3. **Naturally acquired HPV antibodies against subsequent homotypic infection: A large-scale prospective cohort study,**Xingmei Yao, Wen Chen, Chao Zhao, Lihui Wei, Yuemei Hu, Mingqiang Li, Zhijie Lin, Bizhen Lin, Xiaohui Liu, Ying Hong, Qing Li, Qinjing Pan, Xun Zhang, Mingzhu Li, Yuqian Zhao, Li Zhang, Huifang Xu, Fangfang Hu, Jun Zhao, Yue Huang, Wei Sheng, Ya Zheng, Shangying Hu, Yingying Su, Shoujie Huang, Huirong Pan, Fanghui Zhao, Youlin Qiao, Ting Wu, Jun Zhang, Ningshao Xia,The Lancet Regional Health - Western Pacific,Volume 13,2021,100196,https://doi.org/10.1016/j.lanwpc.2021.100196.

Summary

Background

Although recent studies have suggested that naturally acquired Human papillomavirus (HPV) antibodies are partly protective against subsequent homotypic infection, the extent of protection remains indecisive. Here, we evaluate the protective effect of neutralizing and IgG antibodies simultaneously.

Methods

In a cohort of 3634 women aged 18-45 years from the control arm of a phase III trial of the HPV-16/18 bivalent vaccine, participants were tested for neutralizing antibodies by pseudovirion-based neutralization assay (PBNA) and IgG antibodies by enzyme-linked immunosorbent assay (ELISA) at baseline. HPV-16/18 incident and persistent infections were identified using cervical specimens periodically collected during the 5·5 years of follow-up. The protective effects of HPV-16/18 neutralizing and IgG antibodies against homotypic infection were assessed using a Cox proportional hazard model.

Findings

For the persistent infection (PI) endpoints of HPV-16/18 lasting for over 6/12 months, a prevalence of type-specific neutralizing antibodies was highly protective (6-month PI: hazard ratio (HR) = 0·16, 95% confidence interval (CI): 0·04, 0·65; 12-month PI: HR = 0·23, 95% CI: 0·06, 0·94), whereas a prevalence of IgG antibodies was associated with minor and non-significant protection (6-month PI: HR = 0·66, 95% CI: 0·40, 1·09; 12-month PI: HR = 0·66, 95% CI: 0·36, 1·20). After increasing the cut-off value to the median IgG level, the risk of 6-month PI was significantly lower in seropositive vs seronegative women (HR = 0·38, 95% CI: 0·18, 0·83).

Interpretation

Naturally acquired antibodies are associated with a substantially reduced risk of subsequent homotypic infection.

Funding

NSFC; The Fujian Province Health Education Joint Research Project; Xiamen Science and Technology Major Project; CIFMS; and Xiamen Innovax.

4. **Emergence of novel hypervirulent Acinetobacter baumannii strain and herpes simplex type 1 virus in a case of community-acquired pneumonia in China,** Qiujing Wang, Haiyang Liu, Yue Yao, Hangfei Chen, Zhejuan Yang, Haibo Xie, Rongna Cui, Huasheng Liu, Chuner Li, Weiping Gong, Yunsong Yu, Xiaoting Hua, Shibo Li,Journal of Infection and Public Health,Volume 17, Issue 7,2024,102456,https://doi.org/10.1016/j.jiph.2024.05.044.

Abstract:

Background

A. baumannii is an important and common clinical pathogen, especially in the intensive care unit (ICU). This study aimed to characterize one hypervirulent A. baumannii strain in a patient with community-acquired pneumonia and herpes simplex type 1 virus infection.

Methods

Minimum inhibitory concentrations (MICs) were determined using the Kirby-Bauer (K-B) and broth microdilution methods. Galleria mellonella infection model experiment was conducted. Whole-genome sequencing (WGS) was performed using the Illumina and Nanopore platforms. The resistance and virulence determinants were identified using the ABRicate program with ResFinder and the VFDB database. The capsular polysaccharide locus (K locus) and lipooligosaccharide outer core locus (OC locus) were identified using Kleborate with Kaptive. Phylogenetic analyses were conducted using the BacWGSTdb server.

Results

A. baumannii XH2146 strain belongs to ST10Pas and ST447Oxf. The strain was resistant to cefazolin, ciprofloxacin, and trimethoprim/sulfamethoxazole (TMP-SMX). Bautype and Kaptive analyses showed that XH2146 contains OCL2 and KL49. WGS analysis revealed that the strain harbored blaADC-76, blaOXA-68, ant(3'')-IIa, tet(B), and sul2. Notably, tet(B) and sul2, both were located within a 114,700-bp plasmid (designated pXH2146–1). Virulence assay revealed A. baumannii XH2146 possessed higher virulence than A. baumannii AB5075 at 12 h. Comparative genomic analysis showed that A. baumannii ST447 strains were mainly isolated from the USA and exhibited a relatively close genetic relationship. Importantly, 11 strains were observed to carry blaOXA-58; blaOXA-23 was identified in 11 isolates and three ST447 A. baumannii strains harbored blaNDM-1.

Conclusions

Early detection of community-acquired hypervirulent Acinetobacter baumannii strains is recommended to prevent their extensive spread in hospitals.

Keywords: Hypervirulent; Acinetobacter baumannii; ST447Oxf; ST10Pas; Genome comparison

5. **Laboratory-acquired infections with Brucella bacteria in China**,Langui Song, Jiangmei Gao, Zhongdao Wu,Biosafety and Health,Volume 3, Issue 2,2021,Pages 101-104,https://doi.org/10.1016/j.bsheal.2020.07.010.

Abstract:

Brucellosis is an important zoonotic infectious disease and is an important public health problem that causes serious economic consequences to the livestock industry. Brucella spp. comprise one of the most common pathogens causing laboratory-acquired infections (LAIs) and are becoming an increasingly important biosafety issue. To understand the significance of Brucella LAIs in China, related papers were search based on three Chinese databases (CNKI, Wanfang, and VIP), as well as PubMed. After assessment, 37 total cases were evaluated, including 27 students, seven laboratory technicians (one pregnant), two housekeeping staff, and one instructor. The age, sex, incubation period, pathogen detection results, and potential routes of infections were collected and analyzed. All LAIs occurred due to improper operations, inadequate biosafety training, and substandard laboratory safety conditions. Therefore, it is urgent to establish a comprehensive and systematic biosafety prevention/control system in laboratories to protect staff members from accidental exposures and LAIs; further, possible risks and control measures for the management of such infections were proposed.

Keywords: Brucella; Laboratory-acquired infection; China

6. **Hospital-acquired bloodstream infections in patients with cancer: current knowledge and future directions**,A. MacPhail, C. Dendle, M. Slavin, Z. McQuilten,Journal of Hospital Infection,Volume 148,2024,Pages 39-50,https://doi.org/10.1016/j.jhin.2024.03.002.

Summary

Patients with cancer experience higher rates of preventable harm from hospital-acquired bloodstream infections (haBSIs) and central-line-associated bloodstream infections (CLABSIs) compared with the general hospital population. The prevention of haBSIs and CLABSIs in patients with cancer is an urgent priority, and requires standardized surveillance and reporting efforts.

The application of haBSI and CLABSI definitions, classification systems and surveillance strategies for patients with cancer is complex, and there is wide variation in clinical practice. Existing systems were not designed explicitly for patients with cancer, and have different strengths and weaknesses in the cancer setting. For these reasons, epidemiological estimates of haBSIs and CLABSIs in patients with cancer also require careful interpretation. This complexity can be a barrier to identifying appropriate targets for intervention and reducing preventable harm. This review provides an overview of key concepts and challenges in haBSI surveillance and prevention specific to patients with cancer. In addition, this review summarizes the strengths and weaknesses of commonly used surveillance definitions and denominators in the setting of cancer care; existing surveillance practice; epidemiology of haBSIs and CLABSIs; prevention strategies; and current knowledge gaps. A global collaborative effort to harmonize the surveillance of hospital-acquired infections in patients with cancer would be invaluable to improve the accuracy and utility of existing data, advance efforts to prevent hospital-acquired infections, and improve patient safety.

Keywords: Healthcare-associated infections; Catheter-related infections; Cancer; Epidemiology

7. **Effect of SARS-CoV-2 infection and pandemic period on healthcare-associated infections acquired in intensive care units,**Alain Lepape, Anaïs Machut, Cedric Bretonnière, Arnaud Friggeri, Charles-Hervé Vacheron, Anne Savey,Clinical Microbiology and Infection,Volume 29, Issue 4,2023,Pages 530-536,https://doi.org/10.1016/j.cmi.2022.10.023.

Abstract:

Objectives

To compare the occurrence of healthcare-associated infections acquired in intensive care units (HAI-ICUs) in France among patients with COVID-19 and those without it in 2020 and the latter with that in patients before the COVID-19 pandemic.

Methods

Multicentre HAI-ICU surveillance network (REA-REZO) data were used to identify 3 groups: 2019 patients (2019Control), a COVID-19 group (2020Cov), and a non–COVID-19 group (2020NonCov). The primary outcome was the occurrence of HAI-ICU (ventilator-associated pneumonia [VAP], bloodstream infections [BSIs], catheter-related bacteraemia). Standardized infection ratios of VAP were calculated for each quarter in 2020 and compared with those in 2019.

Results

A total of 30 105 patients were included in 2020: 23 798 in the 2020NonCov group, 4465 in 2020Cov group, and 39 635 patients in the 2019Control group. The frequency of VAP was strikingly greater in the 2020Cov group: 35.6 (33.4–37.8) episodes/1000 days of mechanical ventilation versus 18.4 (17.6–19.2) in the 2020NonCov group. VAP standardized infection ratio was high in 2020 patients, particularly during the 2 quarters corresponding to the 2 waves. BSI/1000 days were more frequent in the 2020Cov group (6.4% [6.4–6.4%] vs. 3.9% [3.8–3.9%] in the 2020NonCov group). VAP and BSI were also more frequent in the 2020NonCov group than in the 2019Control group. The microbial epidemiology was only slightly different.

Discussion

The data presented here indicate that HAI-ICUs were more frequent during the COVID-19 period, whether the patients were admitted for COVID-19 or, to a lesser extent, for another cause. This implies that managing patients with severe disease in a pandemic context carries risks for all patients.

Keywords: COVID-19; Hospital-acquired infections; Intensive care; Surveillance network; Ventilator-associated pneumonia

8. **A single-center study of patients with rare isolated acquired clotting factor deficiencies other than acquired hemophilia A,**Dandan Yu, Feng Xue, Xiaofan Liu, Yunfei Chen, Rongfeng Fu, Ting Sun, Xinyue Dai, Mankai Ju, Huan Dong, Renchi Yang, Wei Liu, Lei Zhang,Research and Practice in Thrombosis and Haemostasis,Volume 8, Issue 6,2024,102554,https://doi.org/10.1016/j.rpth.2024.102554.

Abstract:

Background

Isolated acquired clotting factor deficiencies (ACFDs) are mainly caused by the existence of anti-factor antibodies or adsorption of clotting factors onto substances such as amyloid. Besides acquired factor (F)VIII deficiency (acquired hemophilia A), the remaining factor deficiencies are rare and diverse, posing challenges in both diagnosis and management.

Objectives

To describe different features of isolated ACFDs to improve our understanding of these diseases and provide practical recommendations for their management.

Methods

Clinical characteristics of patients with isolated acquired FII, FV, FIX, FX, FXI, FXII, FXIII, and von Willebrand factor deficiencies were collected from a single center between July 1997 and December 2021 and analyzed retrospectively.

Results

A total of 54 rare isolated ACFD patients were enrolled in our study, mainly including 20 acquired FV deficiency patients and 16 acquired FX deficiency patients. The median age at diagnosis of all rare isolated ACFD patients was 55 years. The median time to diagnose all rare isolated ACFD patients was 60 days. Ten (18.5%) rare isolated ACFD patients had no bleeding and 2 (3.7%) rare isolated ACFD patients showed venous thromboembolism. Hemostatic treatment was applied to 41 (41/54; 75.9%) rare isolated ACFD patients. Thirty-seven (68.5%) rare isolated ACFD patients received immunosuppressive therapy, and 10 (18.5%) rare isolated ACFD patients received chemotherapy targeting primary diseases. Twenty-two (61.9%) rare isolated ACFD patients achieved complete remission, and 9 (21.4%) rare isolated ACFD patients died.

Conclusion

Rare isolated ACFDs are underestimated, associated with delayed diagnosis, and lack effective therapy. Clinicians should raise awareness for recognizing and managing rare isolated ACFD patients to avoid morbidity and mortality.

Keywords: acquired clotting factor deficiency; bleeding; diagnosis; inhibitor; immunosuppression

9. **Does a patient with acquired arbovirus infection have a hearing impairment? A scoping review of hearing changes in an adult with Dengue, Chikungunya, and Zika,**Leonardo Gleygson Angelo Venâncio, Lilian Ferreira Muniz, Lais Cristine Delgado da Hora, Jéssica Dayane da Silva, Gabriela Silva Teixeira Cavalcanti, Mariana de Carvalho Leal, Sílvio da Silva Caldas Neto,Brazilian Journal of Otorhinolaryngology,Volume 90, Issue 1,2024,101342,https://doi.org/10.1016/j.bjorl.2023.101342.

Abstract:

Objectives

To identify and understand the evidence regarding hearing changes related to acquired Dengue, Chikungunya, and Zika virus infection in adult individuals.

Methods

A scoping review was performed according to the recommendations of The Joanna Briggs Institute and guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews in the Embase, PubMed/Medline, ScienceDirect, Scopus, and Web of Science databases without restriction on language and year of publication. Case studies, observational studies, and clinical trials reporting hearing loss in adult subjects (>18–60 years of age) of both sexes with DENV, CHIKV, or ZIKV diagnosed by positive molecular/serological examination by RT-PCR or IgM/IgG by ELISA method were included.

Results

Thirteen studies met the inclusion criteria and were selected for review. The occurrence of auditory symptoms caused by arboviroses and the presence of permanent or transient sensorineural hearing loss was variable in adults.

Conclusions

Dengue, Chikungunya, and Zika infections in adults are associated with a variety of auditory symptoms. The frequency of permanent or transient sensorineural hearing loss is low but not negligible.

Keywords: Zika virus; Chikungunya virus; Dengue; Hearing disorders; Auditory perceptual disorders

10. **Real world impact of emicizumab & immunosuppression on Acquired Hemophilia A: A Multicenter US Cohort,**Jacqueline N Poston, Cassandra Bryan, Annette von Drygalski, Kadhim Al Banaa, Jenny Y Zhou, Aric Parnes, Evan C Chen, Osman Khan, Patrick Ellsworth, Lorraine Cafuir, Christopher Walsh, Miguel A Escobar, James F Wu, Lynn M Malec, Craig M Kessler, Maissaa Janbain, Rebecca Kruse-Jarres,Blood Advances,2024,https://doi.org/10.1182/bloodadvances.2024013882.

Abstract:

Acquired Hemophilia A (AHA) is an autoimmune bleeding disorder from anti-factor VIII (FVIII) antibodies with high morbidity and mortality due to bleeding and complications from immunosuppression (IST). To address the real-world implications of the FVIII mimetic antibody, emicizumab, and the role of IST, we retrospectively collected deidentified data on 62 AHA patients treated with off label emicizumab for a median of 10 weeks at 12 US hemophilia treatment centers. Most patients (95.2%) had acute bleeding at diagnosis with 62.9% having

partial or no control of bleeds despite use of hemostatic agents at the time emicizumab was started. The main reason for initiating emicizumab was outpatient bleeding prophylaxis. After initiation of emicizumab, 87.1% had no additional bleeds. There were 6 breakthrough bleeds (2 spontaneous) in 5 patients and no fatal bleeding events on maintenance emicizumab. The mean breakthrough bleed rate per patient-week was 0.02 (95% CI 0.0 – 0.03) during the first 12 weeks of emicizumab for the 55 patients with at least 12 weeks of follow up. Of these patients, 92.7% received IST with 74.5% given rituximab-based regimens. Complete resolution of inhibitor and normalization of FVIII levels occurred in 56% overall and 63% of the patients treated with rituximab. Overall, the median time to discontinue emicizumab and IST was 18 weeks. Two patients had thrombotic events on emicizumab, but no adverse events were attributed to emicizumab and there were no infections due to IST. Emicizumab provides effective outpatient bleeding prophylaxis for AHA, and concurrent IST may further mitigate bleeding.

Keywords: Acquired Hemophilia A; Emicizumab; Immunosuppression

11. **Practices to prevent non-ventilator hospital-acquired pneumonia: a narrative review,**A. Livesey, S. Quarton, H. Pittaway, A. Adiga, F. Grudzinska, D. Dosanjh, D. Parekh,Journal of Hospital Infection,Volume 151,2024,Pages 201-212,https://doi.org/10.1016/j.jhin.2024.03.019.

Summary

Nosocomial infection has significant consequences in health care, both at the individual level due to increased morbidity and mortality, and at the organizational level due to increased costs. Hospital-acquired pneumonia (HAP) is the most common nosocomial infection, and is associated with high excess mortality, frequent use of broad-spectrum antimicrobials and increased length of stay. This review explores the preventative strategies that have been examined in non-ventilator HAP (NV-HAP). The management of aspiration risk, interventions for oral hygiene, role of mobilization and physiotherapy, modification of environmental factors, and vaccination are discussed. Many of these interventions are low risk, acceptable to patients and have good cost–benefit ratios. However, the evidence base for prevention of NV-HAP is weak. This review identifies the lack of a unified research definition, under-recruitment to studies, and variation in intervention and outcome measures as limitations in the existing literature. Given that the core risk factors for acquisition of NV-HAP are increasing, there is an urgent need for research to address the prevention of NV-HAP. This review calls for a unified definition of NV-HAP, and identification of a core outcome set for studies in NV-HAP, and suggests future directions for research in NV-HAP. Improving care for people with NV-HAP will reduce morbidity, mortality and healthcare costs significantly.

Keywords: Non-ventilator hospital-acquired pneumonia; NVHAP; Hospital-acquired pneumonia; HAPNosocomial pneumonia; Nosocomial infection; Prevention strategies

12. **Lipidomic and metabolomic changes in community-acquired and COVID-19 pneumonia,** Mireia Saballs, Sandra Parra, Neus Martínez, Nuria Amigo, Lydia Cabau, Simona Iftimie, Raul Pavon, Xavi Gabaldó, Xavier Correig, Silvia Paredes, Josep Maria Vallvé, Antoni Castro,Journal of Lipid Research,Volume 65, Issue 9,2024,100622,https://doi.org/10.1016/j.jlr.2024.100622.

Abstract:

This prospective observational study compared the 1H NMR blood lipidomes and metabolomes of 71 patients with community-acquired pneumonia (CAP), 75 patients with COVID-19 pneumonia, and 75 healthy controls (matched by age and sex) to identify potential biomarkers and pathways associated with respiratory infections. Both pneumonia groups had comparable severity indices, including mortality, invasive mechanical ventilation, and intensive care unit admission rates. Patients with COVID-19 pneumonia exhibited more pronounced hypolipidemia, with significantly lower levels of total cholesterol and LDL-c compared to patients with CAP. Atherogenic lipoprotein subclasses (VLDL-cholesterol, IDL-cholesterol, IDL-triglyceride, and LDL-triglyceride/LDL-cholesterol) were significantly increased in severe cases of both pneumonia types, while lower HDL-c and small, dense HDL particles were associated with more severe illness. Both infected groups showed decreased esterified cholesterol and increased triglycerides, along with reduced phosphatidylcholine, lysophosphatidylcholine, PUFA, omega-3 fatty acids, and DHA. Additionally, infected patients had elevated levels of glucose, lactate, 3-hydroxybutyrate, and acetone, which are linked to inflammation, hypoxemia, and sepsis. Increased levels of branched-chain amino acids, alanine, glycine, and creatine, which are involved in energy metabolism and protein catabolism, were also observed. Neurotransmitter synthesis metabolites like histidine and glutamate were higher in infected patients, especially those with COVID-19. Notably, severe infections showed a significant decrease in glutamine, essential for lymphocyte and macrophage energy. The severity of COVID-19 pneumonia was also associated with elevated glycoprotein levels (glycoprotein A, glycoprotein B, and glycoprotein F), indicating an inflammatory state. These findings suggest that metabolomic and lipidomic changes in pneumonia are connected to bioenergetic pathways regulating the immune response.

Keywords: lipidomics; metabolomics; COVID-19; HDL; NMR; pneumonia

13. **The burden of hospital acquired infections and antimicrobial resistance,** Molly Kukua Abban, Eunice Ampadubea Ayerakwa, Lydia Mosi, Abiola Isawumi,Heliyon,Volume 9, Issue 10,2023,e20561,https://doi.org/10.1016/j.heliyon.2023.e20561.

Abstract:

The burden of Hospital care-associated infections (HCAIs) is becoming a global concern. This is compounded by the emergence of virulent and high-risk bacterial strains such as "ESKAPE" pathogens – (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species), especially within Intensive care units (ICUs) that house high-risk and immunocompromised patients. In this review, we discuss the contributions of AMR pathogens to the increasing burden of HCAIs and provide insights into AMR mechanisms, with a particular focus on last-resort antibiotics like polymyxins. We extensively discuss how structural modifications of surface-membrane lipopolysaccharides and cationic interactions influence and inform AMR, and subsequent severity of HCAIs. We highlight some bacterial phenotypic survival mechanisms against polymyxins. Lastly, we discuss the emergence of plasmid-mediated resistance as a phenomenon making mitigation of AMR difficult, especially within the ICUs. This review provides a balanced perspective on the burden of HCAIs, associated pathogens, implication of AMR and factors influencing emerging AMR mechanisms.

Keywords: Hospital care-associated infections; Nosocomial infections; Antimicrobial resistance; ESKAPE pathogens; AMR mechanisms; Polymyxins

14. **Safety and efficacy of omadacycline for treatment of community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections in patients with mild-to-moderate renal impairment,** Oliver A. Cornely, Thomas M. File, Lynne Garrity-Ryan, Surya Chitra, Robert Noble, Paul C. McGovern,International Journal of Antimicrobial Agents,Volume 57, Issue 2,2021,106263,https://doi.org/10.1016/j.ijantimicag.2020.106263.

Abstract:

Background

Many antibiotics require dosage adjustments in patients with renal impairment. In Phase III studies, omadacycline was non-inferior to moxifloxacin and linezolid in adults with community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections

(ABSSSI), respectively. This analysis evaluated efficacy and safety measures from three omadacycline studies by patient renal function.

Methods

Patients were stratified as having normal renal function (creatinine clearance >89 mL/min), mild renal impairment (creatinine clearance 60–89 mL/min) or moderate renal impairment (creatinine clearance <60 mL/min); creatine clearance ≤30 mL/min (severe renal impairment) was an exclusion criterion. Efficacy endpoints were clinical success at the early clinical response (ECR) and post-treatment evaluation (PTE) time-points. Safety was evaluated as treatment-emergent adverse events (TEAEs) and laboratory measures.

Results

This subgroup analysis included 773 patients with CABP and 1339 patients with ABSSSI in intent-to-treat (ITT) and modified ITT populations, respectively. Clinical success rates were high at ECR and PTE across the studies (CABP 75–90%; ABSSSI 74–95%), and broadly similar between treatments, irrespective of renal function. Rates of TEAEs in patients with ABSSSI ranged from 33% to 52%, and were similar across renal function groups. In patients with CABP, higher rates were observed in patients with moderate renal impairment (56–61%) compared with patients with normal renal function or mild renal impairment (35–49%). The most common TEAEs were nausea and vomiting.

Conclusions

Clinical success was similar across renal function groups, indicating no notable difference in the efficacy of omadacycline in patients with mild or moderate renal impairment. Omadacycline and comparators displayed similar safety profiles.

ClinicalTrials.gov registry

OPTIC (NCT02531438); OASIS-1 (NCT02378480); OASIS-2 (NCT02877927).

Keywords: Community-acquired bacterial pneumonia; Omadacycline; Renal impairment; Skin infection

15. **Epidemiology and prevention of hospital-acquired carbapenem-resistant Enterobacterales infection in hospitalized patients, Northeast Ethiopia**,Agumas Shibabaw, Zenawork Sahle, Yeshi Metaferia, Asgdew Atlaw, Behailu Adenew, Alemu Gedefie, Mihret Tilahun, Endris Ebrahim, Yeshimebet Kassa, Habtu Debash, Shu-Hua Wang,IJID Regions,Volume 7,2023,Pages 77-83,https://doi.org/10.1016/j.ijregi.2023.02.008.

Abstract:

Objective

Carbapenemase-producing carbapenem-resistant Enterobacterales (CP-CRE) are usually healthcare associated. The aim of this study was to investigate the epidemiology of hospital-acquired CRE and multi-drug-resistant infections, and identify associated risk factors in hospitalized patients in Northeast Ethiopia.

Methods

This cross-sectional study was conducted in patients admitted with sepsis between January and June 2021. Demographic and clinical data were collected using questionnaires. In total, 384 samples were collected and cultured based on source of infection. Bacterial species identification was performed using biochemical tests, and drug susceptibility testing was done using the Kirby–Bauer disk diffusion method. The modified carbapenem inactivation method was employed for carbapenemase detection. Data were analysed using Statistical Package for the Social Sciences.

Results

The overall rate of CP-CRE infection was 14.6%. Bloodstream infections and urinary tract infections were the predominant hospital-acquired infections (HAIs). The majority of CP-CRE were Escherichia coli and Klebsiella pneumoniae, and accounted for 4.9%. Chronic underlying disease (adjusted odds ratio (AOR): 7.9, 95% confidence interval (CI): 1.9–31.5), number of beds per room (AOR: 11, 95% CI: 1.7–75) and eating raw vegetables (AOR: 11, 95% CI: 3.4–40) were significantly associated with hospital-acquired CRE infection.

Conclusions

The rate of CP-CRE infection found in this study is concerning. There is a need for further evaluation of risk factors and measures to decrease HAI. Hand hygiene, increased laboratory capacity, improved infection prevention measures, and antimicrobial stewardship programmes are needed in healthcare settings to halt the transmission of CP-CRE.

Keywords: Carbapenemase-producing Enterobacterales; Carbapenem-resistant Enterobacterales; Hospitalized patients; Hospital-acquired infection

16. **Association between tocilizumab treatment of hyperinflammatory patients with COVID-19 in a critical care setting and elevated incidence of hospital-acquired bacterial and invasive fungal infections**,B. Minihan, E. McAuliffe, J. Powell, S.L. Wong, K. Wilkie, C. Murphy, A. Maher, L. Power, N.H. O'Connell, C.P. Dunne,Journal of Hospital Infection,Volume 126,2022,Pages 29-36,https://doi.org/10.1016/j.jhin.2022.04.007.

Summary

Background

Tocilizumab is an interleukin-6 inhibitor that reduces mortality and the need for invasive mechanical ventilation, while increasing the possibility of successful hospital discharge for hyperinflammatory patients with severe coronavirus disease 2019 (COVID-19). No increase in adverse events or serious infections has been reported previously.

Aim

To describe the characteristics and outcomes of patients with severe COVID-19 in critical care who received tocilizumab, and to compare mortality and length of hospital stay for patients who received tocilizumab (N=41) with those who did not (N=33).

Methods

Retrospective review of data related to patients with COVID-19 who received tocilizumab in a critical care setting from 1st January to 31st December 2021.

Findings

Amongst COVID-19 survivors, those who had received tocilizumab had longer intensive care unit (ICU) stays (median length 21 vs 9 days) and hospital stays (45 vs 34 days) compared with those who had not received tocilizumab. Thirty-day mortality (29% vs 36%; P=0.5196) and 60-day mortality (37% and 42%; P=0.6138) were not significantly lower in patients who received tocilizumab. Serious bacterial and fungal infections occurred at higher frequency amongst patients who received tocilizumab [odds ratio (OR) 2.67, 95% confidence interval (CI) 1.04–6.86; P=0.042], and at significantly higher frequency than in non-COVID-19 ICU admissions (OR 5.26, 95% CI 3.08–9.00; P<0.0001).

Conclusions

In this single-centre study, patients in critical care with severe COVID-19 who received tocilizumab had a greater number of serious bacterial and fungal infections, but this may not have been a direct effect of tocilizumab treatment.

Keywords: COVID-19; Tocilizumab; COVID-19 secondary infections; COVID-19 mortality

17. **Intracellular infection and immune system cues rewire adipocytes to acquire immune function**,George Caputa, Mai Matsushita, David E. Sanin, Agnieszka M. Kabat, Joy Edwards-Hicks, Katarzyna M. Grzes, Roland Pohlmeyer, Michal A. Stanczak, Angela Castoldi, Jovana Cupovic, Aaron J. Forde, Petya Apostolova, Maximilian Seidl, Nikki van Teijlingen Bakker, Matteo Villa, Francesc Baixauli, Andrea Quintana, Alexandra Hackl, Lea Flachsmann, Fabian Hässler, Jonathan D. Curtis, Annette E. Patterson, Philipp Henneke, Erika L. Pearce, Edward J. Pearce,Cell Metabolism,Volume 34, Issue 5,2022,Pages 747-760.e6,https://doi.org/10.1016/j.cmet.2022.04.008.

Summary

Adipose tissue (AT) plays a central role in systemic metabolic homeostasis, but its function during bacterial infection remains unclear. Following subcutaneous bacterial infection, adipocytes surrounding draining lymph nodes initiated a transcriptional response indicative of stimulation with IFN-γ and a shift away from lipid metabolism toward an immunologic function. Natural killer (NK) and invariant NK T (iNKT) cells were identified as sources of infection-induced IFN-γ in perinodal AT (PAT). IFN-γ induced Nos2 expression in adipocytes through a process dependent on nuclear-binding oligomerization domain 1 (NOD1) sensing of live intracellular bacteria. iNOS expression was coupled to metabolic rewiring, inducing increased diversion of extracellular L-arginine through the arginosuccinate shunt and urea cycle to produce nitric oxide (NO), directly mediating bacterial clearance. In vivo, control of infection in adipocytes was dependent on adipocyte-intrinsic sensing of IFN-γ and expression of iNOS. Thus, adipocytes are licensed by innate lymphocytes to acquire anti-bacterial functions during infection.

Keywords: perinodal adipose tissue; adipocyte; lymph node; infection; NOS2; NOD1; IFN-γ; NK cells; iNK T cells; metabolism

18. **Emicizumab versus immunosuppressive therapy for the management of acquired hemophilia A**,Christina Hart, Robert Klamroth, Ulrich J. Sachs, Richard Greil, Paul Knoebl, Johannes Oldenburg, Wolfgang Miesbach, Christian Pfrepper, Karolin Trautmann-Grill, Isabell Pekrul, Katharina Holstein, Hermann Eichler, Carmen Weigt, Dorothea Schipp, Sonja Werwitzke, Andreas Tiede,Journal of Thrombosis and Haemostasis,Volume 22, Issue 10,2024,Pages 2692-2701,https://doi.org/10.1016/j.jtha.2024.06.010.

Abstract:

Background

Acquired hemophilia A (AHA) is an autoimmune bleeding disorder caused by neutralizing antibodies against coagulation factor VIII. Immunosuppressive therapy (IST) is standard of care to eradicate autoantibody production and protect from further bleeding but carries a risk of severe infection and mortality in frail patients with AHA. Recently, emicizumab has been studied for its potential to reduce the need for early and aggressive IST.

Objectives

To compare outcomes of 2 studies that used either IST (GTH-AH 01/2010; N = 101) or prophylaxis with emicizumab (GTH-AHA-EMI; N = 47) early after diagnosis of AHA.

Methods

Baseline characteristics were balanced by propensity score matching. Primary endpoint was the rate of clinically relevant new bleeds during the first 12 weeks; secondary endpoints were adverse events and overall survival.

Results

The negative binominal model–based bleeding rate was 68% lower with emicizumab as compared with IST (incident rate ratio, 0.325; 95% CI, 0.182-0.581). No difference was apparent in the overall frequency of infections (emicizumab 21%, IST 29%) during the first 12 weeks, but infections were less often fatal in emicizumab-treated patients (0%) compared with IST-treated patients (11%). Thromboembolic events occurred less often with emicizumab (2%) than with IST (7%). Overall survival after 24 weeks was better with emicizumab (90% vs 76%; hazard ratio, 0.44; 95%, CI, 0.24-0.81).

Conclusion

Using emicizumab instead of IST in the early phase after initial diagnosis of AHA reduced bleeding and fatal infections and improved overall survival.

Keywords: autoimmune hemophilia; bispecific antibody; bleeding; immunosuppression; inhibitor

19. **Efficacy of a fixed-dose combination injectable (0.2 mg/kg doramectin + 6.0 mg/kg levamisole hydrochloride) in Australian cattle against naturally acquired gastrointestinal nematode infections**,Raj Packianathan, Andrew Hodge, Jacqueline Wright, Michael Pearce, Andrew A. DeRosa,Veterinary Parasitology,Volume 323, Supplement,2023,110025,https://doi.org/10.1016/j.vetpar.2023.110025.

Abstract:

Australian producers have long used macrocyclic lactones (MLs) to successfully control cattle gastrointestinal nematodes (GINs) and consequently improve production parameters. However, the trajectory of ML resistance development in cattle GINs is following that of small ruminant nematode populations, highlighting a need for novel treatment options to provide efficacy in the current environment and interrupt the long-term establishment of ML-resistant GIN populations in Australian cattle. Here, we describe three field studies conducted in Australia to evaluate the efficacy of a single administration of a novel fixed-dose combination injectable (FDCI) endectocide against naturally acquired infections of cattle GINs. The FDCI is administered subcutaneously to deliver 0.2 mg/kg doramectin and 6 mg/kg levamisole hydrochloride (HCl). Study sites consisted of three farms in New South Wales (n = 2) and Victoria (n = 1). At each site, cattle were randomly allocated into one of three treatment groups: (1) untreated control (saline), (2) FDCI (0.2 mg/kg doramectin, 6 mg/kg levamisole HCl) or (3) positive control (0.2 mg/kg ivermectin). All treatments were administered on Day 0. Fecal samples were collected prior to treatment on Days −1 (Study 3) or 0 (Studies 1 and 2) and again on Day 14 (post-treatment) to evaluate efficacy via fecal egg count (FEC) and for coproculture. Adequacy of infection was confirmed at all three study sites, with Day 14 geometric mean (GM) FECs for saline-treated cattle ranging from 32.5 eggs per gram (EPG) to 623.7 EPG. FECs for FDCI-treated cattle were significantly reduced compared to saline-treated cattle ($p \leq 0.0001$) on Day 14, with GM-based efficacy ≥ 99.7% at all three study sites. In contrast, ivermectin was 97.4% effective against cattle GINs in Study 1 but was only 47.2% and 39.8% effective at study site 2 and 3, respectively. Genus-specific efficacies suggest the presence of ivermectin-resistant Cooperia spp. (Study 1), Haemonchus spp. (Study 2) and Ostertagia spp. (Study 3) populations in the naturally infected cattle used in these studies. The post-treatment FEC and genus-specific efficacy estimations indicate the doramectin + levamisole HCl FDCI was highly efficacious against cattle GINs even in the face of ivermectin LOE at study sites 2 and 3. The efficacy of the new FDCI against both ML-susceptible and ML-resistant economically important cattle GINs in Australia affirms it is a valuable treatment option for producers operating in an environment of ML loss of efficacy.

Keywords: Anthelmintic; Cooperia; Dectomax V®; Doramectin; Gastrointestinal nematode; Haemonchus; Levamisole; Macrocyclic lactone; Ostertagia; Resistance; Trichostrongylus

20. **Mycobacterium tuberculosis is less likely to acquire pathogenic mutations during latent infection than during active disease,** Asami Osugi, Aki Tamaru, Takashi Yoshiyama, Tomotada Iwamoto, Satoshi Mitarai, Yoshiro Murase, Florence Claude Doucet-Populaire, Microbiology Spectrum, Volume 12, Issue 7, 2024, https://doi.org/10.1128/spectrum.04289-23.

Abstract:

Most people infected with Mycobacterium tuberculosis (Mtb) are believed to be in a state of latent tuberculosis (TB) infection (LTBI). Although LTBI is asymptomatic and not infectious, there is a risk of developing active disease even decades after infection. Here, to characterize mutations acquired during LTBI, we collected and analyzed Mtb genomes from seven Japanese patient pairs, each pair consisting of two active TB patients whose starting dates of developing active disease were >3 years apart; one had a high suspicion of LTBI before developing active disease, whereas the other did not. Thereafter, we compared these genomes with those of longitudinal sample pairs within a host of chronic active TB infections combined with public data. The bacterial populations in patients with LTBI were genetically more homogeneous and accumulated single nucleotide polymorphisms (SNPs) slower than those from active disease. Moreover, the lower proportion of nonsynonymous SNPs indicated weaker selective pressures during LTBI than active disease. Finally, the different mutation spectrums indicated different mutators between LTBI and active disease. These results suggest that the likelihood of the acquisition of mutations responsible for antibiotic resistance and increased virulence was lower in the Mtb population from LTBI than active disease. IMPORTANCE Controlling latent tuberculosis (TB) infection (LTBI) activation is an effective strategy for TB elimination, where understanding Mycobacterium tuberculosis (Mtb) dynamics within the host plays an important role. Previous studies on chronic active disease reported that Mtb accumulated genomic mutations within the host, possibly resulting in acquired drug resistance and increased virulence. However, several reports suggest that fewer mutations accumulate during LTBI than during the active disease, but the associated risk is largely unknown. Here, we analyzed the genomic dynamics of Mtb within the host during LTBI. Our results statistically suggest that Mtb accumulates mutations during LTBI, but most mutations are under low selective pressures, which induce mutations responsible for drug resistance and virulence. Thus, we propose that LTBI acts as a source for new TB disease rather than as a period for in-host genome evolution.

Controlling latent tuberculosis (TB) infection (LTBI) activation is an effective strategy for TB elimination, where understanding Mycobacterium tuberculosis (Mtb) dynamics within the host plays an important role. Previous studies on chronic active disease reported that Mtb accumulated genomic mutations within the host, possibly resulting in acquired drug resistance and increased virulence. However, several reports suggest that fewer mutations accumulate during LTBI than during the active disease, but the associated risk is largely unknown. Here, we analyzed the genomic dynamics of Mtb within the host during LTBI. Our results statistically suggest that Mtb accumulates mutations during LTBI, but most mutations are under low selective pressures, which induce mutations responsible for drug resistance and virulence. Thus, we propose that LTBI acts as a source for new TB disease rather than as a period for in-host genome evolution.

Keywords: latent infection; Mycobacterium tuberculosis; adaptive mutations

21. **Sex differences in aged 80 and over hospitalized patients with community-acquired UTI: A prospective observational study,**Ian López-Cruz, Ana Esparcia, Manuel Madrazo, Juan Alberola, José María Eiros, Arturo Artero,Heliyon,Volume 8, Issue 10,2022,e11131,https://doi.org/10.1016/j.heliyon.2022.e11131.

Abstract:

Aim

This study aimed to evaluate clinically significant sex differences that could have an effect on the choice of treatment and outcomes of urinary tract infection (UTI) in aged 80 and over hospitalized patients with community-acquired UTI.

Methods

This was a prospective study of 161 patients aged 80 and over admitted to hospital with community-acquired UTI. Epidemiological, clinical, laboratory and microbiologic variables were compared between both sexes. Multivariate analysis was performed using logistic regression to determine the variables independently associated with sex.

Results

In a population of 91 (56.52%) women and 70 (43.48%) men, aged 80 and over, we found that women were more likely to have cognitive impairment ($p = 0.035$) and less likely to have chronic obstructive pulmonary disease (COPD) ($p = 0.006$) and indwelling urinary catheter ($p < 0.001$) than men. Levels of creatinine were higher in men than in women ($p = 0.008$). Septic shock at

presentation was more frequent in the male group (p = 0.043). Men had a higher rate of polymicrobial infection (p = 0.035) and Pseudomonas aeruginosa infection (p = 0.003). Factors independently associated with sex by multivariate analysis were septic shock, cognitive impairment, COPD and indwelling urinary catheter.

Conclusion

Men aged 80 and over with community-acquired UTI had more septic shock at admission to hospital and higher rates of indwelling urinary catheter, while women had more cognitive impairment. There were no differences in outcomes between sexes.

Keywords: Aged 80 and over; Community acquired infections; Sex differences; Sepsis; Urinary tract infection

22. **The burden of hospital-acquired infections (HAI) in sub-Saharan Africa: a systematic review and meta-analysis,** Herbert Melariri, Robert Freercks, Elizabeth van der Merwe, Wilma Ten Ham-Baloyi, Opeoluwa Oyedele, Richard A. Murphy, Clarissa Claasen, Paschal Emeka Etusim, Maureen Okam Achebe, Shadrach Offiah, Paula E. Melariri,eClinicalMedicine,Volume 71,2024,102571,https://doi.org/10.1016/j.eclinm.2024.102571.

Summary

Background

Hospital-acquired infections (HAI) are a leading cause of morbidity and mortality globally. These infections are diverse, but the majority are lower respiratory tract infection (LRTI), surgical site infection (SSI), bloodstream infection (BSI), and urinary tract infection (UTI). For most sub-Saharan African countries, studies revealing the burden and impact of HAI are scarce, and few systematic reviews and meta-analysis have been attempted. We sought to fill this gap by reporting recent trends in HAI in sub-Saharan Africa (SSA) with attention to key patient populations, geographic variation, and associated mortality.

Methods

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we conducted a literature search of six electronic databases (Web of Science, Pubmed, APA PsycInfo, CINAHL, Embase, and the Cochrane Library) to identify studies assessing the prevalence of HAI in SSA countries. Studies published between 01 January 2014 and 31 December 2023 were included. We applied no language or publication restrictions. Record

screening and data extractions were independently conducted by teams of two or more reviewers. Using the R software (version 4.3.1) meta and metafor packages, we calculated the pooled prevalence estimates from random-effect meta-analysis, and further explored sources of heterogeneity through subgroup analyses and meta-regression. This study is registered with PROSPERO, CRD42023433271.

Findings

Forty-one relevant studies were identified for analysis, consisting of 15 from West Africa (n = 2107), 12 from Southern Africa (n = 2963), 11 from East Africa (n = 2142), and 3 from Central Africa (n = 124). A total of 59.4% of the patient population were associated with paediatric admissions. The pooled prevalence of HAI was estimated at 12.9% (95% CI: 8.9–17.4; n = 7336; number of included estimates [k] = 41, $p < 0.001$). By subregions, the pooled current prevalence of HAI in the West Africa, Southern Africa, East Africa and Central Africa were estimated at 15.5% (95% CI: 8.3–24.4; n = 2107; k = 15), 6.5% (95% CI: 3.3–10.7; n = 2963; k = 12), 19.7% (95% CI: 10.8–30.5; n = 2142; k = 11) and 10.3% (95% CI: 1.1–27.0; n = 124; k = 3) of the patient populations respectively. We estimated mortality resulting from HAI in SSA at 22.2% (95% CI: 14.2–31.4; n = 1118; k = 9).

Interpretation

Our estimates reveal a high burden of HAI in SSA with significant heterogeneity between regions. Variations in HAI distribution highlight the need for infection prevention and surveillance strategies specifically tailored to enhance prevention and management with special focus on West and East Africa, as part of the broader global control effort.

Funding

No funding was received for this study.

Keywords: Hospital-acquired infections; Nosocomial; Trends; Healthcare; Burden; Sub-Saharan Africa

23. **Hepatitis E virus: do locally acquired infections in Australia necessitate laboratory testing in acute hepatitis patients with no overseas travel history?, 1 NN**Ashish C. Shrestha, Helen M. Faddy, Robert L.P. Flower, Clive R. Seed, Anthony J. Keller,Pathology,Volume 47, Issue 2,2015,Pages 97-100,https://doi.org/10.1097/PAT.0000000000000229.

Summary

Hepatitis E virus (HEV) is emerging as a global public health threat. Water-borne HEV outbreaks are common in developing countries and are associated with genotypes 1 and 2. In industrialised countries, sporadic cases of zoonotic transmission associated with genotypes 3 and 4 are increasingly being reported. Transfusion- and transplantation-transmitted HEV have been documented, although ingestion of contaminated food is thought to be the major transmission route. Severe disease is possible and chronic hepatitis infection occurs in solid-organ-transplant recipients andin patients with immunosuppressive disorders. In Australia, HEV cases are mainly travellers returning from disease endemic countries. Indeed, there are few reported cases of locally acquired HEV. Pigs in Australia have been shown to be infected with HEV, which indicates the possibility of zoonotic transmission. The extent of locally acquired infection is not known, however it may be greater than expected and may necessitate laboratory testing in patients reporting no overseas travel.

Keywords: Acute hepatitis; Australia; chronic hepatitis; hepatitis E virus; laboratory testing; seroprevalence; traveller; zoonotic

24. **Prevalence of ESKAPE pathogens in the environment: Antibiotic resistance status, community-acquired infection and risk to human health,**Julia Denissen, Brandon Reyneke, Monique Waso-Reyneke, Benjamin Havenga, Tobias Barnard, Sehaam Khan, Wesaal Khan,International Journal of Hygiene and Environmental Health,Volume 244,2022,114006,https://doi.org/10.1016/j.ijheh.2022.114006.

Abstract:

The ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.) pathogens are characterised by increased levels of resistance towards multiple classes of first line and last-resort antibiotics. Although these pathogens are frequently isolated from clinical environments and are implicated in a variety of life-threatening, hospital-associated infections; antibiotic resistant ESKAPE strains have been isolated from environmental reservoirs such as surface water, wastewater, food, and soil. Literature on the persistence and subsequent health risks posed by

the ESKAPE isolates in extra-hospital settings is however, limited and the current review aims to elucidate the primary reservoirs of these pathogens in the environment, their antibiotic resistance profiles, and the link to community-acquired infections. Additionally, information on the current state of research regarding health-risk assessments linked to exposure of the ESKAPE pathogens in the natural environment, is outlined.

Keywords: ESKAPE pathogens; Environment; Antibiotic resistance; Community-acquired infection; Risk assessment

25. **Novel scores relevant to antimicrobial resistance and hospital-acquired infections developed with data from a multi-hospital consortium in the Parisian region of France,**R. Amarsy, B. Granger, S. Fournier, C. Monteil, D. Trystram, V. Siorat, V. Jarlier, J. Robert, Laurence Armand Lefevre, Alexandra Aubry, Véronique Avettand-Fenoel, Frédéric Barbut, Laurent Belec, Béatrice Bercot, Stéphane Bonacorsi, Vincent Calvez, Emmanuelle Cambau, Etienne Carbonnelle, Charlotte Charpentier, Stéphane Chevaliez, Jean-Winoc Decousser, Constance Delaugerre, Diane Descamps, Laurent Dortet, Florence Doucet-Populaire, Pierre Frange, Slim Fourati, Jean-Louis Gaillard, Elyanne Gault, Jean-Louis Herrmann, Vincent Jarlier, Solen Kerneis, Jérôme Le Goff, Jean-Luc Mainardi, Anne-Geneviève Marcelin, Laurence Morand-Joubert, Jean-Michel Pawlotsky, Claire Poyart, Marie-Anne Rameix-Welti, Jérôme Robert, Christophe Rodriguez, Anne-Marie Roque Afonso, Martin Rottman, Flore Rozenberg, Etienne Ruppé, David Skurnik, Nicolas Veziris, Jean-Ralph Zahar, Guilene Barnaud, Typhaine Billard-Pomares, Gaëlle Cuzon, Dominique Decré, Alexandra Doloy, Jean-Luc Donay, Laurence Drieux-Rouzet, Isabelle Durand, Agnès Ferroni, Vincent Fihman, Nicolas Fortineau, Camille Gomart, Nathalie Grall, Christelle Guillet-Caruba, Françoise Jaureguy, Valérie Lalande, Luce Landraud, Véronique Leflon, Patricia Mariani, Liliana Mihaila, Didier Moissenet, Latifa Noussair, Isabelle Podglajen, Isabelle Poilane, Hélène Poupet, Emilie Rondinaud, Valérie Sivadon Tardy, David Trystram, Charlotte Verdet, Emmanuelle Vigier, Sophie Vimont-Billarant,Journal of Hospital Infection,Volume 143,2024,Pages 97-104,https://doi.org/10.1016/j.jhin.2023.09.022.

Summary

Purpose

Indicators for comparing and understanding differences in antimicrobial resistance (AMR) and healthcare-associated infections (HAIs) for benchmarking are essential to identify priorities for hospitals.

Methods

This study measured the incidence of hospital-acquired or resistant Gram-negative bacilli bloodstream infections (GNB-BSIs) in a large public healthcare consortium in the Parisian region of France.

Results

Within each hospital, there was a strong positive correlation between the incidence of GNB-BSIs due to resistant GNB and the incidence of hospital-acquired GNB-BSIs. Two scores measuring AMR and HAI rates by combining different GNB-BSI incidence rates were developed as indicators. These scores were highly variable within the hospital consortium. On multi-variate analysis, AMR and HAI scores were significantly associated with the proportion of surgical beds, staff absenteeism and the consumption of alcohol-based hand rub, with the latter two characteristics being amenable to interventions. Carbapenem use was also linked to AMR, but this may be because carbapenems are the preferred drug for treating resistant infections.

Conclusion

These results shed light on the incidence of HAIs and AMR in the study hospitals, and suggest possibilities for targeted interventions at healthcare facility level.

Keywords: Antimicrobial resistance; Healthcare-associated infection; Bloodstream infection; Hand hygiene; Antibiotic consumption; Hospital organization

26. **Trends in pediatric ambulatory community acquired infections before and during COVID-19 pandemic: A prospective multicentric surveillance study in France,** Pr Robert Cohen, Alexis Rybak, Andreas Werner, Stéphane Béchet, Roxane Desandes, Fréderic Hassid, Jean-Marie André, Nathalie Gelbert, Georges Thiebault, Fabienne Kochert, Fabienne Cahn-Sellem, François Vié Le Sage, Pr François Angoulvant, Naïm Ouldali, Bruno Frandji, Corinne Levy,The Lancet Regional Health - Europe,Volume 22,2022,100497,https://doi.org/10.1016/j.lanepe.2022.100497.

Summary

Background

Covid-19 pandemic control has imposed several non-pharmaceutical interventions (NPIs). Strict application of these measures has had a dramatic reduction on the epidemiology of several infectious diseases. As the pandemic is ongoing for more than 2 years, some of these measures have been removed, mitigated, or less well applied. The aim of this study is to investigate the

trends of pediatric ambulatory infectious diseases before and up to two years after the onset of the pandemic.

Methods

We conducted a prospective surveillance study in France with 107 pediatricians specifically trained in pediatric infectious diseases. From January 2018 to April 2022, the electronic medical records of children with an infectious disease were automatically extracted. The annual number of infectious diseases in 2020 and 2021 was compared to 2018-2019 and their frequency was compared by logistic regression.

Findings

From 2018 to 2021, 185,368 infectious diseases were recorded. Compared to 2018 (n=47,116) and 2019 (n=51,667), the annual number of cases decreased in 2020 (n=35,432) by about a third. Frequency of scarlet fever, tonsillopharyngitis, enteroviral infections, bronchiolitis, and gastroenteritis decreased with OR varying from 0·6 (CI95% [0·5;0·7]) to 0·9 (CI95% [0·8;0·9]), p<0·001. In 2021, among the 52,153 infectious diagnoses, an off-season rebound was observed with increased frequency of enteroviral infections, bronchiolitis, gastroenteritis and otitis with OR varying from 1·1 (CI95% [1·0;1·1]) to 1·5 (CI95% [1·4;1·5]), p<0·001.

Interpretation

While during NPIs strict application, the overall frequency of community-acquired infections was reduced, after relaxation of these measures, a rebound of some of them (enteroviral infections, bronchiolitis, gastroenteritis, otitis) occurred beyond the pre-pandemic level. These findings highlight the need for continuous surveillance of infectious diseases, especially insofar as future epidemics are largely unpredictable.

Funding

ACTIV, AFPA, GSK, MSD, Pfizer and Sanofi.

Keywords: Ambulatory network; Covid-19 pandemic; Children; Immunity debt

27. **Hypoalbuminemia as predictor of thrombotic events in patients with community-acquired pneumonia,**Emanuele Valeriani, Roberto Cangemi, Roberto Carnevale, Giulio Francesco Romiti, Arianna Pannunzio, Pasquale Pignatelli, Francesco Violi,International Journal of Cardiology,Volume 404,2024,131942,https://doi.org/10.1016/j.ijcard.2024.131942.

Abstract:

Background

Hypoalbuminemia complicates acute diseases and infections and is associated with a worst prognosis. The aim is to evaluate whether hypoalbuminemia is associated with higher incidence and risk of thrombotic events in community-acquired pneumonia.

Methods

We retrospectively collected data from a prospective study investigating the incidence of thrombotic events in community-acquired pneumonia hospitalized patients from 2011 to 2016 at University-Hospital Policlinico Umberto I. Baseline characteristics and outcomes were collected. Incidence of outcomes were calculated. Kaplan-Meier curves were created, Cox model used to identify predictors for the outcomes, and competing risk analysis performed.

Results

From a total of 231 patients, 130 (56.3%) and 101 (43.7%) had or not hypoalbuminemia. Age, proportion of female, BMI, major comorbidities, and severity of pneumonia were similar between two subgroups. A less proportion of patients with hypoalbuminemia received antithrombotic and statin therapy. Median hospital stay was 11 days in both subgroups. Patients with hypoalbuminemia had higher D-dimer and high- sensitivity C-reactive-protein values with an inverse relation between albumin values and these markers. Incidence of thrombotic events was 26 and 11 per 1000 patient-days in patient with and without hypoalbuminemia. At Cox model, hypoalbuminemia was associated with thrombotic events development in univariable (hazard ratio; 2.67, 95% confidence intervals, 1.30–5.40) and multivariable (hazard ratio 3.19; 95% confidence intervals, 1.48–6.89) analysis.

Conclusions

More than a half of patients with community acquired pneumonia had hypoalbuminemia that is associated with a doubled incidence and a three-fold increased risk of thrombotic events. The inverse relation between baseline albumin and D-dimer values confirms this association.

Keywords: Cardiovascular diseases; Hypoalbuminemia; Pneumonia; Serum albumin; Thrombosis

28. **Laboratory Acquired Infection with Recombinant Vaccinia Virus Containing an Immunomodulating Construct,**Martin Mempel, Gisela Isa, Norbert Klugbauer, Hermann Meyer, Gregor Wildi, Johannes Ring, Franz Hofmann, Heidelore Hofmann,Journal of Investigative Dermatology,Volume 120, Issue 3,2003,Pages 356-358,https://doi.org/10.1046/j.1523-1747.2003.12074.x.

Abstract:

Handling of Vaccinia virus represents a risk for laboratory-acquired infections, especially in individuals without completed vaccination. We report the case of a Vaccinia infection in a previously vaccinated researcher working with various genetically modified strains. We could confirm the infection by electron microscopy, positive cell culture, virus-specific PCR, sequence analysis, and viral neutralization test. The isolated virus carried a functionally inactivated cytohesin-1 gene of human origin, which had been shown to impair leukocyte adhesion by interacting with the LFA/ICAM-1 axis. The immunomodulating nature of the inserted construct might thus have added to the infectivity of the virus. We emphasize on the necessity of Vaccinia vaccination in laboratory staff working in the field.

Keywords: Vaccinia virus; vaccination; cytohesin-1 gene

29. **Association between blood culture turnaround time and clinical prognosis in emergency department patients with community acquired bloodstream infection: A retrospective study based on electronic medical records,**Po-Hsiang Hsu, Renin Chang, Chun-Hao Yin, Yao-Shen Chen, Jin-Shuen Chen,Heliyon,Volume 10, Issue 6,2024,e27957,https://doi.org/10.1016/j.heliyon.2024.e27957.

Abstract:

Importance

Previous investigations have found that time to positive blood culture (TTP) is a prognostic factor for clinical outcomes. In fact, what the emergency physician sees from the medical information system is TAT (turnaround time) defined as time required to post a bacterial culture report. We propose a definition of blood culture TAT that more closely aligns with clinical considerations by measuring the time from starting specimen culture to the release of an official blood culture report. We were curious to know whether the duration of TAT is as intricately linked to the prognosis of bacteremia as TTP.

Objectives

To examine the association between TAT and outcomes of adult patients who present to the ED with community acquired bacteremia.

Design

Setting, and Participants: This retrospective study utilized electronic medical records from Kaohsiung Veterans General Hospital (KVGH), a 1000-bed tertiary medical center in Taiwan. Patients were adults aged 18 years and older who presented to ED (Emergency department) for initial diagnosis of community acquired bacteremia from January 1, 2016 to March 31, 2021. Data analysis was performed from December 2022 to January 2023. Main outcomes and measures. The primary outcomes included mortality in the ED, all-cause in-hospital mortality, length of hospital stay, and all-cause 30-day mortality in relation to the individual first report of positive blood culture TAT.

Results

A total of 4011 eligible patients with bacteremia were evaluated, of which 207 patients had a blood culture TAT of ≤48 h. The overall 30-day all-cause mortality rate was 13%. Contrary to expectation, no statistically significant differences were observed in clinical prognosis between the TAT groups (≤48 versus >48 h). Subgroup analyses indicated that the length of TAT did not have a significant effect on clinical prognosis in patients who underwent lactate level assessment. Furthermore, no difference in clinical outcome was noted between TAT groups (≤48 versus >48 h) in terms of Gram-negative bacilli or Gram-positive cocci bacteremia. However, in patients with delayed antibiotic treatment (>3 h), a shorter TAT was significantly associated with a fatal outcome.

Conclusion

In adults with community-acquired bacteremia, this study did not observe a significant association between blood culture TAT and clinical prognosis, except in cases of delayed antibiotic treatment.

30. **Colostrum supplement, immune variables and hospital-acquired infection in acute respiratory failure: A double-blind, randomized, placebo-controlled study**,Elham Roohelhami, Seyed Hossein Ardehali, Elham Makiabadi, Zahra Vahdat Shariatpanahi,Journal of Functional Foods,Volume 111,2023,105909,https://doi.org/10.1016/j.jff.2023.105909.

Abstract:

Background

Bovine colostrum has anti-microbial and immunomodulatory properties. We investigated the possibility of colostrum supplementation for managing hospital-acquired infections in critically ill patients.

Materials & methods

Patients with enteral nutrition were randomly assigned to receive either colostrum 30 g daily in the intervention group or a similar amount of formula in the control group for ten days.

Results

GEE-analysis showed that patients in the colostrum group (n = 45) had higher serum CD4 and CD8 protein levels by 0.33 ng/ml and 0.29 ng/ml respectively than the control group (n = 45) during the study period ($P < 0.05$). The increase of lymphocytes was higher in the colostrum group (ß= 322, $P = 0.04$). The incidence of ventilator-associated pneumonia (7% vs 16%) and clostridium difficile diarrhea (4% vs 22%) were significantly lower in the colostrum group than the control group.

Conclusion

Colostrum increased lymphocytes and serum levels of CD4 and CD8 proteins and reduced the incidence of nosocomial infections.

Keywords: Nosocomial infection; Bovine colostrum; Immunity; T cells; Pneumonia

31. **Immunovirological status in people with perinatal and adult-acquired HIV-1 infection: a multi-cohort analysis from France**,Rémonie Seng, Pierre Frange, Albert Faye, Catherine Dollfus, Jérôme le Chenadec, Faroudy Boufassa, Asma Essat, Tessa Goetghebuer, Elisa Arezes, Véronique Avettand-Fènoël, Jean-Joël Bigna, Stéphane Blanche, Cécile Goujard, Laurence Meyer, Josiane Warszawski, Jean-Paul Viard, H. Aumaitre, E. Froguel, F. Caby, S. Dellion, L. Gerard, F. Lucht, C. Chirouze, M. Dupon, Jl Schmit, C. Goujard, T. Allegre, B. Cazenave, G. Hittinger, P. De Truchis, J. Cailhol, C. Duvivier, A. Canestri, O. Bouchaud, M. Karmochkine, D. Salmon-Ceron, D. Zucman, E. Mortier, R. Tubiana, P.M. Girard, C. Pintado, A. Cabie, V. Rabier, P. Morlat, D. Neau, C. Genet, D. Makhloufi, S Bregigeon Ronot, J. Ghosn, V. Reliquet, P. Perré, Jl Pellegrin, C. Arvieux, C. Cheneau, L. Bernard, P. Delobel, R. Verdon, C. Jacomet, L. Piroth, F. Ajana, S. Bevilacqua, Y. Debab, A.L. Lecapitaine, L. Cotte, S. Mokhtari, P. Mercie, P. Poubeau, V. Garrait, Ma Khuong, G. Beck-Wirth, L. Blum, S. Blanche, F. Boccara, T. Prazuck, C. Barbuat, J.P. Viard, S. Stegmann-Planchard, B. Martha, J.M. Treluyer, E. Dore, C. Gaud, M. Niault, E. Fernandes, H. Hitoto, A. Compagnucci, N. Elenga, A. Faye, C. Dollfus, A. Chace, M. Levine, S.A. Martha, C. Floch-Tudal, K. Kebaïli, N. Entz-Werle, J. Tricoire, F. Mazingue, P. Bolot, P. Brazille, T. Goetghebuer, A.F. Gennotte, D. Van Der Linden, V. Schmitz, M. Moutschen, C. Crenn-Hebert, F. Habibi, A. Coursol, E. Guesdon, P.F. Ceccaldi, M. Dehlinger – Paul, E. Pannier, V. Marcou, J. Ghosn, V. Garrait, C. Elleau, M. Achkar, P. Delobel, M.O. Vareil, A. Chace, S. Couderc, C. Routier, M.A. Bouldouyre, F. Caby, L. Selleret, P. Bolot, A. Chabrol, C. Bellahcene, C. Pluchart, R. Tubiana, A. Yangui, D. Vignes, A. Alissa, A. Johnson, E. Lachassinne, A. Benbara, L. Karaoui, A. Bongain, B. Yakeu, J.L. Schmit, L. Cravello, C. Hubert, C. Dollfus, P. Faucher, D. Pinquier, C. Borie, D. Rocchi, C. Chirouze, C. Brunet-Cartier, C. Briandet, J. Brouard, A. Chalvon-Demersay, M. Rajguru, L. Bernard, K. Billiemaz, A. Fresard, A. Moulin, P. Fialaire, L. Mesnard, E. Werner, E. Vintejoux, J. Marian, S. Ranaivojaona, F. Bissuel, M. Abdelhadi, Y. Hammou, C. Genet-Villeger, Y. Hatchuel, N. Elenga, G. Hittinger, G. Bachelard, M. Medus, J. Dendale – Nguyen, T.S. Guimard, A. Martha, M. Rouha, P. Perfezou, L. De Saint Martin, S. Jaffuel, R. Buzele, C. Arvieux, M. Gousseff, C. Cudeville, M. Niault, V. Vitrat, C. Michau, G. Palenzuela, M. Driessen, B. Heller-Roussin, J.M. Labaune, B. Muanza, G. Hittinger, D. Makhloufi, J. Massardier, M. Partisani, C. Floch-Tudal, V. Marcou, I. Hau, C. Runel-Belliard, C. Brehin, A. Chace, K. Kebaili, M. Lalande, M. Lagree, N. Entz-Werle, K. Lacombe, J.-M. Molina, J. Ghosn, J. Reynes, O. Robineau, F. Raffi, P. Morlat, P. Delobel, A. Becker, C. Goujard, L. Weiss, T. Allègre, G. Pialoux, F. Souala, A. Rami, C. Katlama, A. Cabié, D. Makhloufi, J.-P. Viard, C. Cheneau, F. Bastides, D. Neau, H. Aumaitre, C. Duvivier, O. Bouchaud, P. Fialaire, L. Piroth, C. Michel, D. Salmon, J-D Le Lièvre, G. Hittinger, P. De Truchis, A. Sotto, C. Jacomet, E. Rouveix, A. Naqvi, D. Zucman, S. Brégigeon, R. Rodet, C. Chirouze, A. Simon-Coutelier, V. Garrait, J.-L. Esnault, E. Mortier,

R. Buzelé, S. Bevilacqua, R. Verdon, A. Stein, C. Godin-Colet, G. Pichancourt, A. Chabrol, P. Caraux-Paz, M Mohseni Zadeh, L. Gérard, C. Lascaux-Cametz, L. Bodard, J.-L. Pellegrin, C. Genet, N. Ettahar, A. Uludag, F. Caby, E. Rosenthal, F. Prevoteau du Clary, A. Fresard, S. Jaureguiberry, L. Blum, P. Philibert, A.-L. Lecapitaine, Y. Debab, E. Chakvetadze, H. Champagne, M. Gousseff, E. Froguel, V. Daneluzzi, J. Goupil de Bouillé, A. Leprêtre, I. Lamaury, I. Darasteanu, B. Abraham, D. Garipuy, T. Prazuck, J.-L. Berger, J.-L. Schmit, K. Diallo, F. Gourdon, O. Vaillant, V. Gaborieau, B. Martha, J. Doll, D. Quinsat, L. Geffray, J.-J. Girard, D. Houlbert, C. Michau, B. Cazenave, V. Perronne, E. Klement, O. Antioniotti, C. Rouzioux, V. Avettand-Fenoel, O. Lortholary, J.P. Viard, S. Boucly, A. Maignan, C. Duvivier, R. Thiebaut, L. Meyer, F. Boufassa, M.A. Charles, R. Dray-Spira, C. Legeai, V. Amon, N. Benammar, R. Seng, G. Pialoux, L. Slama, P. Bonnard, C. Chakvetadze, T. L'Yavanc, J. Capeau, C. Vigouroux, S. Fellahi, J.P. Bastard, E. Oksenhendler, L. Gerard, J.F. Bourge, V. Bajzik, D. Sereni, C. Lascoux-Combe, C. Pintado, O. Taulera, L.V. Dien, J. Delgado, J.M. Molina, T. Saint-Marc, S. Ferret, J. Pavie, J.F. Bergmann, A. Rami, M. Parrinello, P.M. Girard, BLefebvre, C. Boudraa, B. Diallo, C. Lupin, S. Herson, A. Simon, N. Edeb, D. Salmon-Ceron, L. Guillevin, T. Tahi, M.P. Pietri, L. Weiss, D. Tisne-Dessus, C. Jalbert, P. Yeni, S. Matheron, G. Pahlavan, B. Phung, N. El-Alami Talbi, Z. Ramani, G. Catalano, C. Godard, F. Boue, V. Chambrin, D. Bornarel, H. Schoen, R. Carlier, B. Fantin, A. Uludag, C. Poder, R. Dhote, M. Bentata, P. Honore, O. Bouchaud, Xuan Tuyet, J.F. Delfraissy, C. Goujard, F. Chaix, M.T. Rannou, Y. Levy, A. Sobel, C. Dumont, A. Cabie, S. Abel, S. Pierre-François, V. Beaujolais, I. Poizot-Martin, O. Zaegel-Faucher, C. Debreux, J. Moreau, S. Mokhtari, E. Van Der Gheynst, M.C. Thiebaut-Drobacheff, A. Foltzer, B. Hoen, J.F. Faucher, H. Gil, M. Dupon, J.M. Ragnaud, I. Raymond, P. Morlat, I. Louis, M. Hessamfar, J. Reynes, V. Baillat, C Merle De Boever, C. Tramoni, A. Soufflet, P. Guadagnin, F. Bastides, P. Choutet, L. Bernard, F. Raffi, O. Mounoury, V. Reliquet, D. Brosseau, H. Hue, T. May, S. Wassoumbou, M. Stenzel, M.P. Bouillon, Y. Yazdanpanah, T. Huleux, E. Aissi, S. Pavel, D. Rey, C. Cheneau, P. Fischer, M. Partisani, G. Blaison, M Mohseni Zadeh, M. Martinot, A. Pachart, F. Jeanblanc, J.L. Touraine, C. Trepo, P. Miailhes, K. Kouadjo, V. Thoirain, C. Brochier, P. Perre, S. Leautez, J.L. Esnault, I. Suaud,The Lancet Regional Health - Europe,Volume 40,2024,100885,https://doi.org/10.1016/j.lanepe.2024.100885.

Summary

Background

No study has compared the virological and immunological status of young people with perinatally-acquired HIV infection (P-HIV) with that of people with HIV adulthood (A-HIV) having a similar duration of infection.

Methods

5 French cohorts of P-HIV and A-HIV patients with a known date of HIV-infection and receiving antiretroviral treatment (ART), were used to compare the following proportions of: virological failure (VF) defined as plasma HIV RNA ≥ 50 copies/mL, CD4 cell percentages and CD4:CD8 ratios, at the time of the most recent visit since 2012. The analysis was stratified on time since infection, and multivariate models were adjusted for demographics and treatment history.

Findings

310 P-HIV were compared to 1515 A-HIV (median current ages 20.9 [IQR:14.4–25.5] and 45.9 [IQR:37.9–53.5] respectively). VF at the time of the most recent evaluation was significantly higher among P-HIV (22.6%, 69/306) than A-HIV (3.3%, 50/1514); p ≤ 0.0001. The risk of VF was particularly high among the youngest children (2–5 years), adolescents (13–17 years) and young adults (18–24 years), compared to A-HIV with a similar duration of infection: adjusted Odds-Ratio (aOR) 7.0 [95% CI: 1.7; 30.0], 11.4 [4.2; 31.2] and 3.3 [1.0; 10.8] respectively. The level of CD4 cell percentages did not differ between P-HIV and A-HIV. P-HIV aged 6–12 and 13–17 were more likely than A-HIV to have a CD4:CD8 ratio ≥ 1: 84.1% vs. 58.8% (aOR = 3.5 [1.5; 8.3]), and 60.9% vs. 54.7% (aOR = 1.9 [0.9; 4.2]) respectively.

Interpretation

P-HIV were at a higher risk of VF than A-HIV with a similar duration of infection, even after adjusting for treatment history, whereas they were not at a higher risk of immunological impairment. Exposure to viral replication among young patients living with HIV since birth or a very early age, probably because of lower adherence, could have an impact on health, raising major concerns about the selection of resistance mutations and the risk of HIV transmission.

Funding

Inserm - ANRS MIE.

Keywords: Perinatal HIV infection; Cohort; Viral failure; Immunological outcome; Epidemiology

32. **Dexamethasone as risk-factor for ICU-acquired respiratory tract infections in severe COVID-19,**Luis Felipe Reyes, Alejandro Rodriguez, Alirio Bastidas, Daniela Parra-Tanoux, Yuli V. Fuentes, Esteban García-Gallo, Gerard Moreno, Gustavo Ospina-Tascon, Glenn Hernandez, Edwin Silva, Ana Maria Díaz, Manuel Jibaja, Magdalena Vera, Emilio Díaz, María Bodí, Jordi Solé-Violán, Ricard Ferrer, Antonio Albaya-Moreno, Lorenzo Socias, Ángel Estella, Ana Loza-Vazquez, Ruth Jorge-García, Isabel Sancho, Ignacio Martin-Loeches,Journal of Critical Care,Volume 69,2022,154014,https://doi.org/10.1016/j.jcrc.2022.154014.

Abstract:

Purpose

Dexamethasone is the only drug that has consistently reduced mortality in patients with COVID-19, especially in patients needing oxygen or invasive mechanical ventilation. However, there is a growing concern about the relation of dexamethasone with the unprecedented rates of ICU-acquired respiratory tract infections (ICU-RTI) observed in patients with severe COVID-19.

Methods

This was a multicenter, prospective cohort study; conducted in ten countries in Latin America and Europe. We included patients older than 18 with confirmed SARS-CoV-2 requiring ICU admission. A multivariate logistic regression and propensity score matching (PSM) analysis was conducted to determine the relation between dexamethasone treatment and ICU-RTI.

Results

A total of 3777 patients were included. 2065 (54.7%) were treated with dexamethasone within the first 24 h of admission. After performing the PSM, patients treated with dexamethasone showed significantly higher proportions of VAP (282/1652 [17.1%] Vs. 218/1652 [13.2%], $p = 0.014$). Also, dexamethasone treatment was identified as an adjusted risk factor of ICU-RTI in the multivariate logistic regression model (OR 1.64; 95%CI: 1.37–1.97; $p < 0.001$).

Conclusion

Patients treated with dexamethasone for severe COVID-19 had a higher risk of developing ICU-acquired respiratory tract infections after adjusting for days of invasive mechanical ventilation and ICU length of stay, suggesting a cautious use of this treatment.

Keywords: Dexamethasone; COVID-19; Critical care; Severe COVID-19; Pneumonia

33. **Clinical study of antibacterial medical textiles containing polyhydroxyalkanoate oligomers for reduction of hospital-acquired infections**,L.L. Ma, Y-Y. Wei, J. Li, Y-Y. Sun, S.R. Liu, K.M. Ma, P.H-M. Leung, X.M. Tao,Journal of Hospital Infection,Volume 149,2024,Pages 144-154,https://doi.org/10.1016/j.jhin.2024.04.009.

Summary

Introduction

The prevention and control of hospital-acquired infections remain a significant challenge worldwide, as textiles used in hospital wards are highly involved in transmission processes. This paper reports a new antibacterial medical fabric used to prepare hospital pillowcases, bottom sheets and quilt covers for controlling and reducing hospital-acquired infections.

Method

The medical fabric was composed of blended yarns of staple polyester (PET) and degradable poly(3-hydroxybutyrate co-3-hydroxyvalerate) (PHBV)/polylactic acid (PLA) fibres, which were coated with polylactide oligomers (PLAO), which are environmentally friendly and safe antimicrobial agents with excellent thermal stability in high-temperature laundry. A clinical trial was conducted, with emphasis on the bacterial species that were closely related to the infection cases in the study hospital.

Result

After 7 days of use, 94% of PET/PHBV/PLA-PLAO fabric retained <20 colony-forming units/100 cm2 of the total bacterial amount, meeting hygiene and cleanliness standards.

Conclusion

This study demonstrates the potential of fabrics containing polyhydroxyalkanoate oligomers as highly effective, safe and long-lasting antimicrobial medical textiles that can effectively reduce the incidence of hospital-acquired infections.

Keywords: Hospital-acquired infections; Antibacterial properties; Thermostability; Poly(3-hydroxybutyrate co-3-hydroxyvalerate)/polylactide fibres; Polylactide oligomers

34. **Bacterial Etiology and Antimicrobial Resistance Pattern of Community-Acquired Urinary Tract Infection in Older Adults**,Aza Bahadeen Taha,Medicine in Microecology,2024,100114,https://doi.org/10.1016/j.medmic.2024.100114.

Abstract:

Background

Urinary tract infections (UTIs) are a significant cause of morbidity in elderly individuals and remain a persistent challenge for medical professionals. This study aimed to identify the bacteria causing community-acquired (CA) UTIs in older patients, determine their antimicrobial resistance patterns, assess the prevalence of polymicrobial infections, and identify the risk factors.

Methods

Urine samples were obtained from patients with symptomatic UTIs and then cultured on blood and MacConkey agar. Positive cultures were identified and tested for antimicrobial susceptibility using the VITEK 2 system.

Results

Polymicrobial infections were found in 69/427 (16.16%) of older patients with CA-UTIs and associated with diabetes ($p = 0.007$), previous antimicrobial use ($p = 0.025$), and recurrent urinary infections ($p = 0.043$). Escherichia coli was the leading pathogen (57.26%), and Klebsiella pneumoniae was identified in 15.32% of CA-UTIs. Escherichia coli was more common in non-diabetic patients (60.81%) than diabetes (43.69%). However, the rates of Klebsiella species were higher in diabetes (20.39%) than non-diabetes (14.50%). Gram-negative uropathogens showed 49.89% resistance to amoxicillin-clavulanic acid, while imipenem is the least resistant (7.19%). The gram-positive uropathogens were resistant to 9.80% of linezolid and highly resistant to erythromycin (74.51%), tetracycline (72.55%), and gentamicin (70.59%).

Conclusions

Escherichia coli isolates were the predominant bacteria in the elderly and highly resistant to amoxicillin-clavulanic. The most effective drug against gram-negative bacteria was imipenem, while linezolid proved potently effective against gram-positive bacteria. Diabetes, previous antimicrobial use, and recurrent urinary infections are risk factors for polymicrobial UTIs.

Keywords: Antibiotic resistance; Recurrent UTIs; Escherichia coli; elderly; polymicrobial infection; VITEK 2

35. **Laboratory-confirmed hospital-acquired infections: An analysis of a hospital's surveillance data in Nigeria**,Garba Iliyasu, Farouq Muhammad Dayyab, Salisu Abubakar, Salisu Inuwa, Sirajo Haliru Tambuwal, Abdulwasiu Bolaji Tiamiyu, Zaiyad Garba Habib, Muktar Ahmed Gadanya, Abdulrahman Abba Sheshe, Muhammad Sani Mijinyawa, Aliyu Aminu, Muhammad Shuaibu Adamu, Kabir Mohammad Mande, Abdulrazaq Garba Habib,Heliyon,Volume 4, Issue 8,2018,e00720,https://doi.org/10.1016/j.heliyon.2018.e00720.

Abstract:

Objective

Hospital-acquired infections (HAI) are a global problem and a major public health concern in hospitals throughout the world. Quantification of HAI is needed in developing countries; hence we describe the results of a 2-year surveillance data in a tertiary hospital in Nigeria.

Methodology

This study is a 2-year review using secondary data collected at a tertiary referral center in northwestern Nigeria. The data was collected using surveillance forms modeled based on the Centre for Disease Control (CDC) protocol. Descriptive statistics were used to present results as frequencies and percentages.

Result

518 patients developed HAI out of 8216 patients giving an overall prevalence of 6.3%. The mean age of the patients was 35.98 years (±15.92). Males constituted 281 (54.2%). UTI 223 (43.1%) was the most prevalent HAI. Overall, E. coli 207 (40.0%) was the most frequent isolates followed by P. aerugenosa 80 (15.4%). There was a high prevalence of cloxacillin resistant S. aureus (67.9%) and gram-negative rods resistant to third-generation cephalosporins. Trimethoprim-sulfamethoxazole resistance across the board was more than 90%.

Conclusion

There is a high burden of HAI especially UTI in our hospital with resistance to commonly used antibiotics documented.

Keywords: Public health; Infectious disease

36. **Increasing trend of healthcare-associated infections due to vancomycin-resistant Enterococcus faecium (VRE-fm) paralleling escalating community-acquired VRE-fm infections in a medical center implementing strict contact precautions: An epidemiologic and pathogenic genotype analysis and its implications**,Ya-Fen Tang, Yin-Shiou Lin, Li-Hsiang Su, Jien-Wei Liu,Journal of Microbiology, Immunology and Infection,Volume 56, Issue 5,2023,Pages 1045-1053,https://doi.org/10.1016/j.jmii.2023.07.015.

Abstract:

Objective

To clarify whether there were clandestine intra-hospital spreads of vancomycin-resistant Enterococcus faecium (VRE-fm) isolates that led to specific strain of VRE lingering in the hospital and/or developing outbreaks that rendered a progressively increasing trend of healthcare-associated infections due to VRE-fm (VRE-fm-HAIs).

Setting

Despite implementing strict contact precautions for hospitalized patients with VRE-fm-infection/colonization, number of VRE-fm-HAIs in a medical centre in southern Taiwan were escalating in 2009–2019, paralleling an increasing trend of community-acquired VRE-fm-infections.

Methods

We analyzed epidemiologic data and genotypes of non-duplicate VRE-fm isolates each grown from a normally sterile site of 89 patients between December 2016 and October 2018; multilocus sequence typing (MLST) and pulse-field gel electrophoresis (PFGE) typing were performed.

Results

Totally 13 sequence types (STs) were found, and the 3 leading STs were ST17 (44%), ST78 (37%), and ST18 (6%); 66 pulsotypes were generated by PFGE. Four VRE-fm isolates grouped as ST17/pulsotype S, 2 as ST17/pulsotype AS, 2 as ST17/pulsotype AU, and 3 as ST78/pulsotype V grew from clinical specimens sampled less than one week apart from patients staying at different wards/departments and/or on different floors of the hospital.

Conclusions

Despite possible small transitory clusters of intra-hospital VRE-fm spreads, there was no specific VRE-fm strain lingering in the hospital leading to increasing trend of VRE-fm-HAIs during the study

period. Strict contact precautions were able to curb intra-hospital VRE-fm spreads, but unable to curb the increasing trend of VRE-fm-HAIs with the backdrop of progressively increasing VRE-fm-infections/colorizations in the community.

Keywords: Vancomycin-resistant Enterococcus; Healthcare-associated infections; Increasing trends; Multilocus sequence typing (MLST); Pulse-field gel electrophoresis typing

37. **Cyclophosphamide vs rituximab for eradicating inhibitors in acquired hemophilia A: A randomized trial in 108 patients**,H. Lévesque, J.F. Viallard, E. Houivet, B. Bonnotte, S. Voisin, V. Le Cam-Duchez, F. Maillot, M. Lambert, E. Liozon, B. Hervier, O. Fain, B. Guillet, J. Schmidt, L.E. Luca, M. Ebbo, N. Ferreira-Maldent, A. Babuty, L. Sailler, P. Duffau, V. Barbay, S. Audia, J. Benichou, J. Graveleau, Y. Benhamou,Thrombosis Research,Volume 237,2024,Pages 79-87,https://doi.org/10.1016/j.thromres.2024.03.012.

Abstract:

Background

Acquired hemophilia A (AHA) is a rare autoimmune disorder due to autoantibodies against Factor VIII, with a high mortality risk. Treatments aim to control bleeding and eradicate antibodies by immunosuppression. International recommendations rely on registers and international expert panels.

Methods

CREHA, an open-label randomized trial, compared the efficacy and safety of cyclophosphamide and rituximab in association with steroids in patients with newly diagnosed AHA. Participants were treated with 1 mg/kg prednisone daily and randomly assigned to receive either 1.5–2 mg/kg/day cyclophosphamide orally for 6 weeks, or 375 mg/m2 rituximab once weekly for 4 weeks. The primary endpoint was complete remission over 18 months. Secondary endpoints included time to achieve complete remission, relapse occurrence, mortality, infections and bleeding, and severe adverse events.

Results

Recruitment was interrupted because of new treatment recommendations after 108 patients included (58 cyclophosphamide, 50 rituximab). After 18 months, 39 cyclophosphamide patients (67.2 %) and 31 rituximab patients (62.0 %) were in complete remission (OR 1.26; 95 % CI, 0.57 to 2.78). In the poor prognosis group (FVIII < 1 IU/dL, inhibitor titer > 20 BU mL−1), significantly

more remissions were observed with cyclophosphamide (22 patients, 78.6 %) than with rituximab (12 patients, 48.0 %; p = 0.02). Relapse rates, deaths, severe infections, and bleeding were similar in the 2 groups. In patients with severe infection, cumulative doses of steroids were significantly higher than in patients without infection (p = 0.03).

Conclusion

Cyclophosphamide and rituximab showed similar efficacy and safety. As first line, cyclophosphamide seems preferable, especially in poor prognosis patients, as administered orally and less expensive.

Funding

French Ministry of Health. ClinicalTrials.gov number: NCT01808911.

Keywords: Acquired hemophilia; Cyclophosphamide; Rituximab; Randomized trial

38. **Immunomodulatory therapy, risk factors and outcomes of hospital-acquired bloodstream infection in patients with severe COVID-19 pneumonia: a Spanish case–control matched multicentre study (BACTCOVID),** Gabriela Abelenda-Alonso, Alexander Rombauts, Carlota Gudiol, Isabel Oriol, Antonella Simonetti, Ana Coloma, Alejandro Rodríguez-Molinero, Elisenda Izquierdo, Vicens Díaz-Brito, Montserrat Sanmartí, Ariadna Padullés, Inmaculada Grau, Mar Ras, Alba Bergas, Lluïsa Guillem, Alejandro Blanco-Arévalo, Claudia Alvarez-Pouso, Natalia Pallarés, Sebastián Videla, Cristian Tebé, Jordi Carratalà,Clinical Microbiology and Infection,Volume 27, Issue 11,2021,Pages 1685-1692,https://doi.org/10.1016/j.cmi.2021.06.041.

Abstract:

Objectives

The effect of the use of immunomodulatory drugs on the risk of developing hospital-acquired bloodstream infection (BSI) in patients with COVID-19 has not been specifically assessed. We aim to identify risk factors for, and outcomes of, BSI among hospitalized patients with severe COVID-19 pneumonia.

Methods

We performed a severity matched case–control study (1:1 ratio) nested in a large multicentre prospective cohort of hospitalized adults with COVID-19. Cases with BSI were identified from the

cohort database. Controls were matched for age, sex and acute respiratory distress syndrome. A Cox proportional hazard ratio model was performed.

Results

Of 2005 patients, 100 (4.98%) presented 142 episodes of BSI, mainly caused by coagulase-negative staphylococci, Enterococcus faecalis and Pseudomonas aeruginosa. Polymicrobial infection accounted for 23 episodes. The median time from admission to the first episode of BSI was 15 days (IQR 9–20), and the most frequent source was catheter-related infection. The characteristics of patients with and without BSI were similar, including the use of tocilizumab, corticosteroids, and combinations. In the multivariate analysis, the use of these immunomodulatory drugs was not associated with an increased risk of BSI. A Cox proportional hazard ratio (HR) model showed that after adjusting for the time factor, BSI was associated with a higher in-hospital mortality risk (HR 2.59; 1.65–4.07; $p < 0.001$).

Discussion

Hospital-acquired BSI in patients with severe COVID-19 pneumonia was uncommon and the use of immunomodulatory drugs was not associated with its development. When adjusting for the time factor, BSI was associated with a higher mortality risk.

Keywords: Bacteraemia; COVID-19; Hospital-acquired infection; SARS-CoV-2 pneumonia; Immunomodulatory therapy

39. **Longitudinal changes in mitochondrial-associated measures and insulin resistance in youth with perinatally-acquired HIV in the U.S,** Greg S. Gojanovich, Wendy Yu, Zhongli J. Zhang, Denise L. Jacobson, Tzy-Jyun Yao, Jennifer Jao, Daniel E. Libutti, Mitchell E. Geffner, Mariana Gerschenson,Mitochondrion,Volume 78,2024,101936,https://doi.org/10.1016/j.mito.2024.101936.

Abstract:

HIV infection and its treatment are associated with mitochondrial dysfunction and metabolic derangement. However, longitudinal changes in oxidative phosphorylation activities [Complex I (C1) and Complex IV (C4)], or venous lactate/pyruvate ratios (LPR), and their relationships with insulin resistance (IR), remain unclear in youth living with perinatally-acquired HIV (YPHIV). We measured venous LPR, C1, and C4 activities in blood cells and homeostatic model assessment for IR (HOMA-IR) over two years. Limited longitudinal differences in mitochondrial-related measures and IR were observed in YPHIV vs youth perinatally HIV-exposed but uninfected. There were no systematic differences in C1, C4, or HOMA-IR between the groups.

Keywords: Insulin resistance; Lactate; Mitochondria; Oxidative phosphorylation; Perinatal HIV; Youth

40. **Differentiation of hypervirulent and classical Klebsiella pneumoniae with acquired drug resistance,**Thomas A. Russo, Cassandra L. Alvarado, Connor J. Davies, Zachary J. Drayer, Ulrike Carlino-MacDonald, Alan Hutson, Ting L. Luo, Melissa J. Martin, Brendan W. Corey, Kara A. Moser, J. Kamile Rasheed, Alison L. Halpin, Patrick T. McGann, Francois Lebreton,mBio,Volume 15, Issue 2,2024,https://doi.org/10.1128/mbio.02867-23.

Abstract:

Distinguishing hypervirulent (hvKp) from classical Klebsiella pneumoniae (cKp) strains is important for clinical care, surveillance, and research. Some combinations of iucA, iroB, peg-344, rmpA, and rmpA2 are most commonly used, but it is unclear what combination of genotypic or phenotypic markers (e.g., siderophore concentration, mucoviscosity) most accurately predicts the hypervirulent phenotype. Furthermore, acquisition of antimicrobial resistance may affect virulence and confound identification. Therefore, 49 K. pneumoniae strains that possessed some combinations of iucA, iroB, peg-344, rmpA, and rmpA2 and had acquired resistance were assembled and categorized as hypervirulent hvKp (hvKp) (N = 16) or cKp (N = 33) via a murine infection model. Biomarker number, siderophore production, mucoviscosity, virulence plasmid's Mash/Jaccard distances to the canonical pLVPK, and Kleborate virulence score were measured and evaluated to accurately differentiate these pathotypes. Both stepwise logistic regression and a CART model were used to determine which variable was most predictive of the strain cohorts. The biomarker count alone was the strongest predictor for both analyses. For logistic regression, the area under the curve for biomarker count was 0.962 (P = 0.004). The CART model generated the classification rule that a biomarker count = 5 would classify the strain as hvKP, resulting in a sensitivity for predicting hvKP of 94% (15/16), a specificity of 94% (31/33), and an overall accuracy of 94% (46/49). Although a count of ≥4 was 100% (16/16) sensitive for predicting hvKP, the specificity and accuracy decreased to 76% (25/33) and 84% (41/49), respectively. These findings can be used to inform the identification of hvKp. IMPORTANCE Hypervirulent Klebsiella pneumoniae (hvKp) is a concerning pathogen that can cause life-threatening infections in otherwise healthy individuals. Importantly, although strains of hvKp have been acquiring antimicrobial resistance, the effect on virulence is unclear. Therefore, it is of critical importance to determine whether a given antimicrobial resistant K. pneumoniae isolate is hypervirulent. This report determined which combination of genotypic and phenotypic markers could most accurately identify hvKp strains with acquired resistance. Both logistic regression and a machine-learning prediction model demonstrated that biomarker count alone was the strongest predictor.

The presence of all five of the biomarkers iucA, iroB, peg-344, rmpA, and rmpA2 was most accurate (94%); the presence of ≥4 of these biomarkers was most sensitive (100%). Accurately identifying hvKp is vital for surveillance and research, and the availability of biomarker data could alert the clinician that hvKp is a consideration, which, in turn, would assist in optimizing patient care.

Hypervirulent Klebsiella pneumoniae (hvKp) is a concerning pathogen that can cause life-threatening infections in otherwise healthy individuals. Importantly, although strains of hvKp have been acquiring antimicrobial resistance, the effect on virulence is unclear. Therefore, it is of critical importance to determine whether a given antimicrobial resistant K. pneumoniae isolate is hypervirulent. This report determined which combination of genotypic and phenotypic markers could most accurately identify hvKp strains with acquired resistance. Both logistic regression and a machine-learning prediction model demonstrated that biomarker count alone was the strongest predictor. The presence of all five of the biomarkers iucA, iroB, peg-344, rmpA, and rmpA2 was most accurate (94%); the presence of ≥4 of these biomarkers was most sensitive (100%). Accurately identifying hvKp is vital for surveillance and research, and the availability of biomarker data could alert the clinician that hvKp is a consideration, which, in turn, would assist in optimizing patient care.

Keywords: Klebsiella; hypervirulent; classical; biomarker; diagnosis

41. **Laboratory-acquired Vibrio cholerae O1 infection in Austria, 2008,** Steliana Huhulescu, Eva Leitner, Gebhard Feierl, Franz Allerberger,Clinical Microbiology and Infection,Volume 16, Issue 8,2010,Pages 1303-1304,https://doi.org/10.1111/j.1469-0691.2009.03051.x.

Abstract:

Vibrio cholerae infection is a rare but well-documented cause of laboratory-associated illness. We report on the first case of indigenous cholera documented in Austria after more than fifty years. In April 2008, the National Reference Centre for V. cholerae received an isolate of V. cholerae O1, serotype Ogawa, cultured from the stool specimen of a patient consulting a general practitioner because of watery diarrhea. The 23 year old microbiology student had been working with viable V. cholerae for 4 weeks in a practical laboratory course. Two days before onset of symptoms an open 300 mL Erlenmeyer flask with approx. 30 mL of overnight V. cholerae culture tipped over and spilled into a laboratory shaker near the student's working place. Wearing gloves and protective gowns, the student and her supervisor immediately cleaned and decontaminated the shaker. As a consequence of this laboratory incident, the institution in question replaced the clamp-less shaker plate by a traditional shaker plate with mechanical clamps.

Keywords: Cholera; clamp-less shaker; laboratory-acquired infection; laboratory shaker; Vibrio cholerae

42. **Perioperative considerations in the paediatric patient with congenital and acquired coagulopathy,** Gabor Erdoes, Susan M. Goobie, Thorsten Haas, Andreas Koster, Jerrold H. Levy, Marie E. Steiner,BJA Open,Volume 12,2024,100310,https://doi.org/10.1016/j.bjao.2024.100310.

Abstract:

Neonates, infants, and children undergoing major surgery or with trauma can develop severe coagulopathy perioperatively. Neonates and infants are at highest risk because their haemostatic system is not fully developed and underlying inherited bleeding disorders may not have been diagnosed before surgery. Historically, laboratory coagulation measurements have been used to diagnose and monitor coagulopathies. Contemporary dynamic monitoring strategies are evolving. Viscoelastic testing is increasingly being used to monitor coagulopathy, particularly in procedures with a high risk of bleeding. However, there is a lack of valid age-specific reference values for diagnosis and trigger or target values for appropriate therapeutic management. A promising screening tool of primary haemostasis that may be used to diagnose quantitative and qualitative platelet abnormalities is the in vitro closure time by platelet function analyser. Targeted individualised treatment strategies for haemostatic bleeding arising from inherited or acquired bleeding disorders may include measures such as tranexamic acid, administration of plasma, derived or recombinant factors such as fibrinogen concentrate, or allogeneic blood component transfusions (plasma, platelets, or cryoprecipitate). Herein we review current recommended perioperative guidelines, monitoring strategies, and treatment modalities for the paediatric patient with a coagulopathy. In the absence of data from adequately powered prospective studies, it is recommended that expert consensus be considered until additional research and validation of goal-directed perioperative bleeding management in paediatric patients is available.

Keywords: bleeding; bleeding disorders; haemostasis; surgery; tranexamic acid; transfusion; trauma; viscoelastic testing

43. **Infection and co-infection patterns of community-acquired pneumonia in patients of different ages in China from 2009 to 2020: a national surveillance study**,Yan-Ning Liu, Yun-Fa Zhang, Qiang Xu, Yan Qiu, Qing-Bin Lu, Tao Wang, Xiao-Ai Zhang, Sheng-Hong Lin, Chen-Long Lv, Bao-Gui Jiang, Hao Li, Zhong-Jie Li, George F Gao, Wei-Zhong Yang, Simon I Hay, Li-Ping Wang, Li-Qun Fang, Wei Liu,The Lancet Microbe,Volume 4, Issue 5,2023,Pages e330-e339,https://doi.org/10.1016/S2666-5247(23)00031-9.

Summary

Background

Severe community-acquired pneumonia (SCAP) is associated with a substantial number of hospitalisations and deaths worldwide. Infection or co-infection patterns, along with their age dependence and clinical effects are poorly understood. We aimed to explore the causal and epidemiological characteristics by age, to better describe patterns of community-acquired pneumonia (CAP) and their association with severe disease.

Methods

National surveillance of CAP was conducted through a network of hospitals in 30 provinces in China from 2009–20 inclusive. Patients with CAP were included if they had evidence of acute respiratory tract, had evidence of pneumonia by chest radiography, diagnosis of pneumonia within 24 h of hospital admission, and resided in the study catchment area. For the enrolled patients with CAP, nasopharyngeal and oral swabs were taken and tested for eight viral pathogens; and blood, urine, or expectorated sputum was tested for six bacterial pathogens. Clinical outcomes, including SCAP, were investigated with respect to age and patterns of infections or co-infections by performing binary logistic regression and multivariate analysis.

Findings

Between January, 2009, and December, 2020, 18 807 patients with CAP (3771 [20·05%] with SCAP) were enrolled. For both children (aged ≤5 years) and older adults (aged >60 years), a higher overall rate of viral and bacterial infections, as well as viral–bacterial co-infections were seen in patients with SCAP than in patients with non-SCAP. For adults (aged 18–60 years), however, only a higher rate of bacterial–bacterial co-infection was observed. The most frequent pathogens associated with SCAP were respiratory syncytial virus (RSV; 21·30%) and Streptococcus pneumoniae (12·61%) among children, and influenza virus (10·94%) and Pseudomonas aeruginosa (15·37%) among older adults. Positive rates of detection of most of the tested pathogens decreased during 2020 compared with the 2009−19 period, except for RSV, P aeruginosa, and Klebsiella pneumoniae. Multivariate analyses showed SCAP was significantly associated with infection with human adenovirus, human rhinovirus, K pneumoniae, or co-

infection of RSV and Haemophilus influenzae or RSV and Staphylococcus aureus in children and adolescents (aged <18 years), and significantly associated with infection with P aeruginosa, K pneumoniae, or S pneumoniae, or co-infection with P aeruginosa and K pneumoniae in adults (aged ≥18 years).

Interpretation

Both prevalence and infection pattern of respiratory pathogens differed between patients with SCAP and patients with non-SCAP in an age-dependent manner. These findings suggest potential advantages to age-related strategies for vaccine schedules, as well as clinical diagnosis, treatment, and therapy.

Funding

China Mega-Project on Infectious Disease Prevention and The National Natural Science Funds of China.

Translation

For the Chinese translation of the abstract see Supplementary Materials section.

44. **Association between acquiring SARS-CoV-2 during pregnancy and post-acute sequelae of SARS-CoV-2 infection: RECOVER electronic health record cohort analysis,** Ann M. Bruno, Chengxi Zang, Zhenxing Xu, Fei Wang, Mark G. Weiner, Nick Guthe, Megan Fitzgerald, Rainu Kaushal, Thomas W. Carton, Torri D. Metz,eClinicalMedicine,Volume 73,2024,102654,https://doi.org/10.1016/j.eclinm.2024.102654.

Summary

Background

Little is known about post-acute sequelae of SARS-CoV-2 infection (PASC) after acquiring SARS-CoV-2 infection during pregnancy. We aimed to evaluate the association between acquiring SARS-CoV-2 during pregnancy compared with acquiring SARS-CoV-2 outside of pregnancy and the development of PASC.

Methods

This retrospective cohort study from the Researching COVID to Enhance Recovery (RECOVER) Initiative Patient-Centred Clinical Research Network (PCORnet) used electronic health record (EHR) data from 19 U.S. health systems. Females aged 18–49 years with lab-confirmed SARS-CoV-

2 infection from March 2020 through June 2022 were included. Validated algorithms were used to identify pregnancies with a delivery at >20 weeks' gestation. The primary outcome was PASC, as previously defined by computable phenotype in the adult non-pregnant PCORnet EHR dataset, identified 30–180 days post-SARS-CoV-2 infection. Secondary outcomes were the 24 component diagnoses contributing to the PASC phenotype definition. Univariable comparisons were made for baseline characteristics between individuals with SARS-CoV-2 infection acquired during pregnancy compared with outside of pregnancy. Using inverse probability of treatment weighting to adjust for baseline differences, the association between SARS-CoV-2 infection acquired during pregnancy and the selected outcomes was modelled. The incident risk is reported as the adjusted hazard ratio (aHR) with 95% confidence intervals.

Findings

In total, 83,915 females with SARS-CoV-2 infection acquired outside of pregnancy and 5397 females with SARS-CoV-2 infection acquired during pregnancy were included in analysis. Non-pregnant females with SARS-CoV-2 infection were more likely to be older and have comorbid health conditions. SARS-CoV-2 infection acquired in pregnancy as compared with acquired outside of pregnancy was associated with a lower incidence of PASC (25.5% vs 33.9%; aHR 0.85, 95% CI 0.80–0.91). SARS-CoV-2 infection acquired in pregnant females was associated with increased risk for some PASC component diagnoses including abnormal heartbeat (aHR 1.67, 95% CI 1.43–1.94), abdominal pain (aHR 1.34, 95% CI 1.16–1.55), and thromboembolism (aHR 1.88, 95% CI 1.17–3.04), but decreased risk for other diagnoses including malaise (aHR 0.35, 95% CI 0.27–0.47), pharyngitis (aHR 0.36, 95% CI 0.26–0.48) and cognitive problems (aHR 0.39, 95% CI 0.27–0.56).

Interpretation

SARS-CoV-2 infection acquired during pregnancy was associated with lower risk of development of PASC at 30–180 days after incident SARS-CoV-2 infection in this nationally representative sample. These findings may be used to counsel pregnant and pregnant capable individuals, and direct future prospective study.

Funding

National Institutes of Health (NIH) Other Transaction Agreement (OTA) OT2HL16184.

Keywords: PASC; Pregnancy; SARS-CoV-2 infection

45. **Clinical characteristics of hospitalized children with community-acquired pneumonia and respiratory infections: Using machine learning approaches to support pathogen prediction at admission,** Tu-Hsuan Chang, Yun-Chung Liu, Siang-Rong Lin, Pei-Hsin Chiu, Chia-Ching Chou, Luan-Yin Chang, Fei-Pei Lai,Journal of Microbiology, Immunology and Infection,Volume 56, Issue 4,2023,Pages 772-781,https://doi.org/10.1016/j.jmii.2023.04.011.

Abstract:

Background

Acute respiratory infections (ARIs) are common in children. We developed machine learning models to predict pediatric ARI pathogens at admission.

Methods

We included hospitalized children with respiratory infections between 2010 and 2018. Clinical features were collected within 24 h of admission to construct models. The outcome of interest was the prediction of 6 common respiratory pathogens, including adenovirus, influenza virus types A and B, parainfluenza virus (PIV), respiratory syncytial virus (RSV), and Mycoplasma pneumoniae (MP). Model performance was estimated using area under the receiver operating characteristic curve (AUROC). Feature importance was measured using Shapley Additive exPlanation (SHAP) values.

Results

A total of 12,694 admissions were included. Models trained with 9 features (age, event pattern, fever, C-reactive protein, white blood cell count, platelet count, lymphocyte ratio, peak temperature, peak heart rate) achieved the best performance (AUROC: MP 0.87, 95% CI 0.83–0.90; RSV 0.84, 95% CI 0.82–0.86; adenovirus 0.81, 95% CI 0.77–0.84; influenza A 0.77, 95% CI 0.73–0.80; influenza B 0.70, 95% CI 0.65–0.75; PIV 0.73, 95% CI 0.69–0.77). Age was the most important feature to predict MP, RSV and PIV infections. Event patterns were useful for influenza virus prediction, and C-reactive protein had the highest SHAP value for adenovirus infections.

Conclusion

We demonstrate how artificial intelligence can assist clinicians identify potential pathogens associated with pediatric ARIs upon admission. Our models provide explainable results that could help optimize the use of diagnostic testing. Integrating our models into clinical workflows may lead to improved patient outcomes and reduce unnecessary medical costs.

Keywords: Machine learning; Children; Respiratory infections; Pathogens prediction; Community-acquired pneumonia

46. **Risk and countermeasure of laboratory-acquired infection based on pathogen transmission routes,**Kunlan Zuo, Zongzhen Wu, Chihong Zhao, Huan Liu,Biosafety and Health,Volume 5, Issue 3,2023,Pages 133-137,https://doi.org/10.1016/j.bsheal.2023.04.006.

Abstract:

Laboratory-acquired infection (LAI) is an important issue in laboratory biosafety for pathogenic microorganism, which aims to prevent the spread of infectious pathogens and protect laboratory personnel from potentially harmful microorganisms. Previous LAI reports provided a source of information for understanding the transmission routes and therapies helping to develop targeted prevention and response programs and to comprehensively ensure the biosafety of laboratories. In this study, from the perspective of the transmission routes of agents, the biosafety risks were discussed from four aspects: skin, eye, or mucous membrane exposure, contaminated sharp inoculation or bites from infected animals and arthropod vectors, ingestion or hand-to-mouth exposure, and inhalation of infectious aerosols. The development and evolution of LAI were reviewed, and appropriate countermeasures and suggestions were proposed accordingly.

Keywords: Laboratory-acquired infection; Transmission route; Biosafety

47. **Mortality due to hospital-acquired infection after cardiac surgery,**Nicolas Massart, Alexandre Mansour, James T. Ross, Caroline Piau, Jean-Philippe Verhoye, Pierre Tattevin, Nicolas Nesseler,The Journal of Thoracic and Cardiovascular Surgery,Volume 163, Issue 6,2022,Pages 2131-2140.e3,https://doi.org/10.1016/j.jtcvs.2020.08.094.

Abstract:

Purpose

Hospital-acquired infections have been associated with significant morbidity and mortality in critically ill surgical patients. However, little is known about mortality due to hospital-acquired infections in cardiac surgery.

Methods

We conducted a retrospective analysis of prospectively collected data from the cardiac surgery unit of a university hospital. All patients who underwent cardiac surgery over a 7-year period were included. Patients with hospital-acquired infections were matched 1:1 with patients with nonhospital-acquired infections based on risk factors for hospital-acquired infections and death after cardiac surgery using propensity score matching. We performed a competitive risk analysis to study the mortality fraction due to hospital-acquired infections.

Results

Of 8853 patients who underwent cardiac surgery, 370 (4.2%) developed 500 postoperative infections (incidence density rate 4.2 hospital-acquired infections per 1000 patient-days). Crude hospital mortality was significantly higher in patients with hospital-acquired infections than in matched patients who did not develop hospital-acquired infections, 15.4% and 5.7%, respectively ($P < .001$). The in-hospital mortality fraction due to hospital-acquired infections in our cohort was 17.1% (12.3%-22.8%). Pseudomonas aeruginosa infection (hazard ratio, 2.09; 95% confidence interval, 1.23-3.49; $P = .005$), bloodstream infection (hazard ratio, 2.08; 95% confidence interval, 1.19-3.63; $P = .010$), and pneumonia (hazard ratio, 1.68; 95% confidence interval, 1.02-2.77; $P = .04$) were each independently associated with increased hospital mortality.

Conclusions

Although hospital-acquired infections are relatively uncommon after cardiac surgery (4.2%), these infections have a major impact on postoperative mortality (attributable mortality fraction, 17.1%).

Keywords: bacteremia; hospital-acquired pneumonia; mortality; propensity score; surgical site infection

48. **Clinical challenge of diagnosing non-ventilator hospital-acquired pneumonia and identifying causative pathogens: a narrative review,** S. Quarton, A. Livesey, H. Pittaway, A. Adiga, F. Grudzinska, A. McNally, D. Dosanjh, E. Sapey, D. Parekh,Journal of Hospital Infection,Volume 149,2024,Pages 189-200,https://doi.org/10.1016/j.jhin.2024.02.029.

Summary

Non-ventilated hospital-acquired pneumonia (NV-HAP) is associated with a significant healthcare burden, arising from high incidence and associated morbidity and mortality. However, accurate identification of cases remains challenging. At present, there is no gold-standard test for the

diagnosis of NV-HAP, requiring instead the blending of non-specific signs and investigations. Causative organisms are only identified in a minority of cases. This has significant implications for surveillance, patient outcomes and antimicrobial stewardship. Much of the existing research in HAP has been conducted among ventilated patients. The paucity of dedicated NV-HAP research means that conclusions regarding diagnostic methods, pathology and interventions must largely be extrapolated from work in other settings. Progress is also limited by the lack of a widely agreed definition for NV-HAP. The diagnosis of NV-HAP has large scope for improvement. Consensus regarding a case definition will allow meaningful research to improve understanding of its aetiology and the heterogeneity of outcomes experienced by patients. There is potential to optimize the role of imaging and to incorporate novel techniques to identify likely causative pathogens. This would facilitate both antimicrobial stewardship and surveillance of an important healthcare-associated infection. This narrative review considers the utility of existing methods to diagnose NV-HAP, with a focus on the significance and challenge of identifying pathogens. It discusses the limitations in current techniques, and explores the potential of emergent molecular techniques to improve microbiological diagnosis and outcomes for patients.

Keywords: Pneumonia; Hospital-acquired pneumonia; Healthcare-associated infection; Diagnosis; Antimicrobial stewardship; Antibiotic resistance

49. **Diagnostic accuracy of point-of-care tests in acute community-acquired lower respiratory tract infections. A systematic review and meta-analysis,** Elisa Gentilotti, Pasquale De Nardo, Eleonora Cremonini, Anna Górska, Fulvia Mazzaferri, Lorenzo Maria Canziani, Mona Mustafa Hellou, Yudith Olchowski, Itamar Poran, Mariska Leeflang, Jorge Villacian, Herman Goossens, Mical Paul, Evelina Tacconelli,Clinical Microbiology and Infection,Volume 28, Issue 1,2022,Pages 13-22,https://doi.org/10.1016/j.cmi.2021.09.025.

Abstract:

Background

Point-of-care tests could be essential in differentiating bacterial and viral acute community-acquired lower respiratory tract infections and driving antibiotic stewardship in the community.

Objectives

To assess diagnostic test accuracy of point-of-care tests in community settings for acute community-acquired lower respiratory tract infections.

Data sources

Multiple databases (MEDLINE, EMBASE, Web of Science, Cochrane Library, Open Gray) from inception to 31 May 2021, without language restrictions.

Study eligibility criteria

Diagnostic test accuracy studies involving patients at primary care, outpatient clinic, emergency department and long-term care facilities with a clinical suspicion of acute community-acquired lower respiratory tract infections. The comparator was any test used as a comparison to the index test. In order not to limit the study inclusion, the comparator was not defined a priori.

Assessment of risk of bias

Four investigators independently extracted data, rated risk of bias, and assessed the quality using QUADAS-2.

Methods of data synthesis

The measures of diagnostic test accuracy were calculated with 95% CI.

Results

A total of 421 studies addressed at least one point-of-care test. The diagnostic performance of molecular tests was higher compared with that of rapid diagnostic tests for all the pathogens studied. The accuracy of stand-alone signs and symptoms or biomarkers was poor. Lung ultrasound showed high sensitivity and specificity (90% for both) for the diagnosis of bacterial pneumonia. Rapid antigen-based diagnostic tests for influenza, respiratory syncytial virus, human metapneumovirus, and Streptococcus pneumoniae had sub-optimal sensitivity (range 49%–84%) but high specificity (>80%).

Discussion

Physical examination and host biomarkers are not sufficiently reliable as stand-alone tests to differentiate between bacterial and viral pneumonia. Lung ultrasound shows higher accuracy than chest X-ray for bacterial pneumonia at emergency department. Rapid antigen-based diagnostic tests cannot be considered fully reliable because of high false-negative rates. Overall, molecular tests for all the pathogens considered were found to be the most accurate.

Keywords: Antibiotic stewardship; Community settings; Community-acquired lower respiratory tract infections; Point-of-care tests

50. **Laboratory-acquired infections and pathogen escapes worldwide between 2000 and 2021: a scoping review,** Stuart D Blacksell, Sandhya Dhawan, Marina Kusumoto, Khanh K Le, Kathrin Summermatter, Joseph O'Keefe, Joseph P Kozlovac, Salama S Almuhairi, Indrawati Sendow, Christina M Scheel, Anthony Ahumibe, Zibusiso M Masuku, Allan M Bennett, Kazunobu Kojima, David R Harper, Keith Hamilton,The Lancet Microbe,Volume 5, Issue 2,2024,Pages e194-e202,https://doi.org/10.1016/S2666-5247(23)00319-1.

Summary

Laboratory-acquired infections (LAIs) and accidental pathogen escape from laboratory settings (APELS) are major concerns for the community. A risk-based approach for pathogen research management within a standard biosafety management framework is recommended but is challenging due to reasons such as inconsistency in risk tolerance and perception. Here, we performed a scoping review using publicly available, peer-reviewed journal and media reports of LAIs and instances of APELS between 2000 and 2021. We identified LAIs in 309 individuals in 94 reports for 51 pathogens. Eight fatalities (2·6% of all LAIs) were caused by infection with Neisseria meningitidis (n=3, 37·5%), Yersinia pestis (n=2, 25%), Salmonella enterica serotype Typhimurium (S Typhimurium; n=1, 12·5%), or Ebola virus (n=1, 12·5%) or were due to bovine spongiform encephalopathy (n=1, 12·5%). The top five LAI pathogens were S Typhimurium (n=154, 49·8%), Salmonella enteritidis (n=21, 6·8%), vaccinia virus (n=13, 4·2%), Brucella spp (n=12, 3·9%), and Brucella melitensis (n=11, 3·6%). 16 APELS were reported, including those for Bacillus anthracis, SARS-CoV, and poliovirus (n=3 each, 18·8%); Brucella spp and foot and mouth disease virus (n=2 each, 12·5%); and variola virus, Burkholderia pseudomallei, and influenza virus H5N1 (n=1 each, 6·3%). Continual improvement in LAI and APELS management via their root cause analysis and thorough investigation of such incidents is essential to prevent future occurrences. The results are biased due to the reliance on publicly available information, which emphasises the need for formalised global LAIs and APELS reporting to better understand the frequency of and circumstances surrounding these incidents.